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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
Graham DAVIS, et al.) Examiner: Melanie J. YU
Application No.: 10/087,730) Group Art Unit: 1641
Filed: March 5, 2002) Confirmation No.: 8527
For: APPARATUS AND METHOD FOR) Appeal No. _____
ANALYTE MEASUREMENT AND) Date: April 12, 2007
IMMUNOASSAY)

SUBSTITUTE BRIEF FOR APPELLANTS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Appeal is from the decision of the Patent Examiner dated March 23, 2006 (paper no. 20032006), rejecting claims 2-36 and 56 for the second time, which are reproduced in Appendix A of this Appeal Brief. The present Substitute Appeal Brief is submitted in response to the Notices of Non-Compliant Appeal Brief mailed on March 13 and 15, 2007.

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I. Real Party in Interest

The entire interest in the present application, and the invention to which it is directed, is assigned to i-STAT Corporation, as recorded in the Patent and Trademark Office at Reel 012694, Frame 0036.

II. Related Appeals and Interferences

The Appellants' legal representative and assignee do not know of any other appeals or interferences that will directly affect, or be directly affected by, or have a bearing on the Board's decision in this Appeal.

III. Status of Claims

The present application contains claims 2-36 and 56, all of which are currently pending. Claims 2-36 and 56 form the basis for this Appeal. Claims 1, 37-55, and 57-62 are canceled.

IV. Status of Amendments

No amendments or responses were filed subsequent to final rejection.

V. Summary of Claimed Subject Matter

The invention relates generally to an apparatus and method for rapid *in situ* determinations of analytes in liquid samples that is capable of being used, for example, in the point-of-care clinical diagnostic field, including use at accident sites, emergency rooms, in surgery, in intensive care units, and also in non-medical environments. [see present application, page 1, lines 5-8]

Conventionally, a multitude of laboratory tests for analytes of interest are performed on biological samples for diagnosis, screening, disease staging, forensic analysis, pregnancy testing, drug testing, and other reasons. While a few qualitative tests, such as pregnancy tests, have been reduced to simple kits for the patient's home use, the majority of quantitative tests still require the expertise of trained technicians in a laboratory setting using sophisticated instruments. Laboratory testing increases the cost of analysis and delays the results. In many circumstances, delay can be detrimental to a patient's condition or prognosis, such as for example the analysis of markers indicating of myocardial infarction. In these critical situations and others, it would be advantageous to be able to perform such analyses at the point of care, accurately, inexpensively, and with a minimum of delay. [see present application, page 1, line 27 – page 2, line 5] Therefore, there exists within the field of analyte sensing, and in particular for applications in which analytes must be determined within biological samples such as blood, a need for apparatus that can rapidly and simply determine analytes at the point-of-care, and can be performed by less highly trained staff than is possible for conventional laboratory-based testing. [see present application, page 5, lines 3-6]

Exemplary embodiments of the present invention are directed to an apparatus and its method of use for determining the presence and/or concentrations of analytes in a liquid sample. More particularly, the invention provides single-use disposable cartridges, adapted for conducting diverse real-time or near real-time assays of analytes. The invention further relates to a cartridge that provides features for processing a metered portion of a sample. The cartridge incorporates features for precise and flexible control of the movement of a sample or a second

fluid within the cartridge, and for the optional amending of sample or fluid with one or more additional reagents or compounds during an assay. While the cartridges of the present invention are intended for use in a reading apparatus, they can also be used separately. The cartridges can comprise conduits, pump means, a fluid, metering means, valves, and an optional sensor or sensors for determining the position or positions of liquids within the conduits. According to particular exemplary embodiments, the present invention relates to the determination of analytes in biological samples such as blood using electrochemical immunosensors or other ligand/ligand receptor-based biosensors. The present invention further relates to a simplified construction of a biosensor, in particular for fabrication of electrochemical immunoassay biosensors capable of determining a wide range of analytes for which receptors or antibodies can be obtained. [see present application, page 1, lines 9-24]

A cartridge according to exemplary embodiments of the present invention has the advantage that the sample and a second fluid can contact the sensor array at different times during an assay sequence. The sample and second fluid can also be independently amended with other reagents or compounds present initially as dry coatings within the respective conduits. Controlled motion of the liquids within the cartridge further permits more than one substance to be amended into each liquid whenever the sample or fluid is moved to a new region of the conduit. In this way, provision is made for multiple amendments to each fluid, greatly extending the complexity of automated assays that can be performed, and therefore enhancing the utility of the present invention. [see present application, page 6, lines 8-15]

Therefore, exemplary embodiments of the present invention provide a flexible analyte analysis system that is capable of adaptation to diverse assay protocols. Control of liquid motion is achieved through coordinated action of pump means, valves, conduit restrictions, air segments, and conductimetric and other sensors. The cartridge can be used in conjunction with a reading device that coordinates liquid movements within the cartridge. Pump means are provided that apply pressure to displace sample and fluid through the conduits of the cartridge. Precise control of the movement of the sample and fluid can be provided by one or more conductimetric sensors disposed within the conduits that sense the presence or absence of a conductive fluid at particular

points. Such information is optionally used to control the pump means. According to additional exemplary embodiments, the cartridge further comprises valves that control the direction of sample and fluid movement. [see present application, page 6, lines 16-26] Features that control the flow of liquids within and between the conduits of the present invention are herein collectively termed “valves.” [see present application, page 7, lines 14-15] For example, in an exemplary embodiment, a valve that closes after contact with a liquid enables one pump to move both the sample and a second liquid sequentially over the analyte sensor array. [see present application, page 6, lines 26-28]

For example, the cartridge can include a closeable valve located between the first conduit and a waste chamber. In such an exemplary embodiment, such a valve can be comprised of a dried sponge material or the like that is coated with an impermeable substance. As illustrated in Figures 4 and 5 of the present application, contacting the sponge material with the sample or a fluid results in swelling of the sponge to fill the cavity, thereby substantially blocking further flow of liquid into the waste chamber. Furthermore, sealing of the opening to the waste chamber upon wetting of the closeable valve provides an airtight seal that blocks the flow of air between the first conduit and the waste chamber to permit the first pump connected to the sample chamber to displace fluid within the second conduit (e.g., to allow fluid in the second conduit to be drawn in contact with the sensor). [see present application, page 15, lines 11-18] According to such an exemplary embodiment, the closeable valve permits the fluid to be displaced in this manner and prevents air from entering the first conduit from the waste chamber. [see present application, page 8, lines 4-5]

Sealing of the opening to the waste chamber upon wetting of the closeable valve also permits the pump to displace fluid from the second conduit into the first conduit in the following manner. After the sample is exposed to the sensor for a controlled time, the sample is moved into a post-analytical conduit where it can be amended with another reagent. It can then be moved back to the sensor and a second reaction period can begin. Alternately, the post-analysis conduit can serve simply to separate the sample segment from the sensor. Within this post-analysis conduit is a single closeable valve that connects the air vent of the sensor conduit to the

diaphragm air pump. When this valve closes, the sample is locked in the post analytical conduit and cannot be moved back to the sensor chip. [see present application, page 15, lines 18-25]

There are several different design examples for such a valve that are encompassed within the present invention. Some designs are activated mechanically while others activate on liquid contact. Other types of closeable valves that are encompassed by the present invention include, but are not limited to: a flexible flap held in an open position by a soluble glue or a gelling polymer that dissolves or swells upon contact with a fluid or sample thus causing the flap to close; and, alternatively, a thin layer of a porous paper or similar material interposed between a conduit and either the waste chamber or ambient air such that the paper is permeable to air while dry but impermeable when wet. In the latter case, it is not necessary that the closeable valve be interposed between a conduit and the waste chamber. The valve passes little to no liquid before closing and so the valve is appropriately placed when positioned between a conduit and the ambient air surrounding the cartridge. For example, in practical construction, a piece of filter paper is placed on an opening in the tape gasket in the fluid path to be controlled. Air can readily move through this media to allow fluid to be moved through the fluid path. When the fluid is pushed over this filter, the filter media becomes filled with liquid and further motion through the fluid path is stopped. Once the filter become wet, significant pressures would be required to move liquid through the pores of the filter. Air flow through the filter is also prevented because of the higher pressure required to push the liquid out of the filter. Such a valve embodiment requires very little liquid to actuate the valve, and actuation occurs rapidly and reliably. [see present application, page 15, line 25- page 16, line 13]

According to an alternative exemplary embodiment, the closeable valve can comprise a mechanical valve. In such an exemplary embodiment, a latex diaphragm can be placed in the bottom of the air bladder on top of a specially constructed well. The well contains two openings that fluidically connect the air vent to the sample conduit. As the analyzer plunger pushes to the bottom of the air bladder, it presses on this latex diaphragm that is adhesive backed and seals the connection between the two holes. This blocks the sample's air vent, locking the sample in place. [see present application, page 16, lines 17-22]

For example, independent claim 2 is directed to a cartridge for sensing at least one analyte in a sample. [*see, e.g.*, page 12, lines 3-5; *see also* Figures 1-5] The cartridge includes a sample holding chamber for receiving the sample and retaining the sample. [*see, e.g.*, page 13, lines 18-20; Figure 4, “conduit 34”] The cartridge includes a first conduit connected to the sample holding chamber. [*see, e.g.*, page 13, lines 1-6; Figure 2, “conduit 15”] The cartridge includes at least one analyte sensor. The sensor comprises an analyte-responsive surface and the surface is within the first conduit. [*see, e.g.*, page 13, lines 19-21; *see also* Figure 4] The cartridge also includes a second conduit for retaining a fluid. The second conduit is connected to the first conduit. [*see, e.g.*, page 13, lines 1-6; Figure 2, “conduit 11”] The cartridge further includes a valve connected to an opening in the first conduit. As discussed previously, the valve is closed by contact with the sample. [*see, e.g.*, page 15, line 11 – page 16, line 22; Figure 5, “valve 58”] The cartridge includes a pump capable of displacing the sample from the holding chamber into the first conduit. The pump is further capable of displacing the fluid from the second conduit into the first conduit. [*see, e.g.*, page 13, line 27 – page 14, line 6; *see also* Figure 4]

For example, independent claim 3 is directed to a cartridge for sensing at least one analyte in a sample. [*see, e.g.*, page 12, lines 3-5; *see also* Figures 1-5] The cartridge includes a sample holding chamber for receiving the sample and retaining the sample. [*see, e.g.*, page 13, lines 18-20; Figure 4, “conduit 34”] The cartridge includes a first conduit connected to the sample holding chamber. [*see, e.g.*, page 13, lines 1-6; Figure 2, “conduit 15”] The cartridge includes at least one analyte sensor. The sensor comprises an analyte-responsive surface and the surface is within the first conduit. [*see, e.g.*, page 13, lines 19-21; *see also* Figure 4] The cartridge also includes a second conduit, connected to the first conduit, for retaining a fluid. [*see, e.g.*, page 13, lines 1-6; Figure 2, “conduit 11”] The cartridge further includes a valve connected to an opening in the first conduit. As discussed previously, the valve is closed by contact with the sample. [*see, e.g.*, page 15, line 11 – page 16, line 22; Figure 5, “valve 58”] The cartridge includes means for inserting at least one air segment into the first or second conduit. For purposes of illustration, the structure described in the specification as corresponding to the

claimed function can be shown as, for example, a pump, such as, for example, the third pump 63 illustrated in Figure 6 and described at page 16, line 29 to pages 17, line 8. The cartridge also includes a pump capable of displacing the sample from the holding chamber into the first conduit, and capable of displacing the fluid from the second conduit into the first conduit. [see, e.g., page 13, line 27 – page 14, line 6; *see also* Figure 4]

Dependent claim 10 recites the feature that the cartridge includes a “metering means for delivering a metered amount of said sample to said at least one analyte sensor.” For purposes of illustration, an exemplary embodiment of the structure described in the specification as corresponding to the claimed function can be shown as, for example, the arrangement illustrated in Figures 1 and 3, and described at page 14, lines 1-6. In particular, the location at which air enters the sample chamber (gasket hole 27 illustrated in Figure 3) from the bladder, and the capillary stop 25, together define a predetermined volume of the sample chamber. An amount of the sample corresponding to this volume can be displaced into the first conduit when paddle 6 (illustrated in Figure 1) is depressed. Such an arrangement is one possible embodiment of a metering means for delivering a metered amount of an unmetered sample into the conduits of the cartridge. [see present application, page 14, lines 1-6]

VI. Grounds of Rejection to be Reviewed on Appeal

The Final Office Action¹ presents one ground of objection and eleven grounds of rejection for review in this Appeal:

1. Claims 46 and 47 are objected to, because the status identifiers for these claims are allegedly unclear.

2. Claims 2, 5, 14, 17, 18, 19, 30, 34, and 56 stand rejected for a second time under 35 U.S.C. § 102(b) as allegedly being anticipated by Schnipelsky et al. (U.S. Patent No. 5,229,297, hereinafter “Schnipelsky”).

3. Claims 3, 6-8, and 12 stand rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Chemelli (U.S. Patent No. 5,254,479, hereinafter “Chemelli”).

4. Claims 4 and 9 stand rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Chemelli, and further in view of Zelin (U.S. Patent No. 5,821,399, hereinafter “Zelin”).

5. Claims 10 and 11 stand rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Opalsky et al. (U.S. Patent No. 6,438,498, hereinafter “Opalsky”).

¹ For the convenience of the Board, attached to the present Appeal Brief as Appendix B is an annotated copy of the Final Office Action in which line numbers have been added to allow convenient reference to passages in the Final Office Action.

6. Claim 13 stands rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Wozniak et al. (U.S. Patent No. 4,781,683, hereinafter “Wozniak”).

7. Claims 15 and 16 stand rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of McNeely et al. (U.S. Patent No. 6,296,020, hereinafter “McNeely”).

8. Claim 20 stands rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Cathey et al. (U.S. Patent No. 5,503,985, hereinafter “Cathey”).

9. Claims 21-26, 28, 29, 32, and 33 stand rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Cathey, and further in view of Zier et al. (U.S. Patent No. 4,919,141, hereinafter “Zier”) and Pourahmadi et al. (U.S. Application Publication No. 2002/0055167, hereinafter “Pourahmadi”).

10. Claim 27 stands rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Cathey, in view of Zier, and in view of Pourahmadi, and further in view of Grundig et al. (U.S. Patent No. 6,221,238, hereinafter “Grundig”).

11. Claims 31 and 36 stand rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Pourahmadi.

12. Claim 35 stands rejected for a second time under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schnipelsky in view of Nelson et al. (U.S. Patent No. 6,074,827, hereinafter “Nelson”).

VII. Arguments

A. Summary of Arguments

For the convenience of the Board, a summary of Appellants' arguments in response to the aforementioned grounds of rejection is provided below. The following arguments are discussed in greater detail in Sections VII.B – VII.D.

1. Objection To Claims 46 And 47, Because The Status Identifiers For These Claims Are Allegedly Unclear.

Contrary to the assertions of the Patent Office, it is respectfully submitted that the status identifiers associated with claims 46 and 47 are clear. However, to resolve any possible confusion on the part of the Patent Office, Appellants respectfully note that claims 46 and 47 are canceled.

2. Rejection Of Claims 2, 5, 14, 17-19, 30, 34, And 56 Under 35 U.S.C. § 102(b) As Allegedly Being Anticipated By Schnipelsky.

These claims recite the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. As illustrated in Figure 1, Schnipelsky teaches that “a one-way check valve (not shown) can be included in passageway [43] to prevent waste liquid from backwashing into compartment 40” [Schnipelsky, column 10, lines 42-45 (emphasis added)] As illustrated in Figure 7, Schnipelsky further teaches that “a check valve 80 can be inserted into passageway 54B to prevent a backwash of DNA into those compartments [(i.e., compartments 30B, 32B, 34B, 36B, 38B, 40B, and 42B)]. Such a valve is conventional, and can comprise, for example, FIG. 8, a seat 82, and a ball 84 which, when pushed back upstream, seats on seat 82 to stop flow. Ball 84 is free, however, to flow downstream up against a small stop 86.” [Schnipelsky, column 14, lines 42-48 (emphasis added)] Contrary to the

assertions of the Patent Office, it is respectfully submitted that the one-way check valves taught by Schnipelsky are not valves that are “closed by contact with the sample.” It is respectfully noted that Schnipelsky teaches that fluid is allowed to pass through the valves when that fluid is in contact with those valves. According to Schnipelsky, it is only when the fluid backwashes do the valves close. Such a manner of operation of the one-way check valve is wholly different than the valve recited in independent claim 2 of the present application.

3. Rejection Of Claims 3, 6-8, And 12 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Chemelli.

These claims recite the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. The combination of Schnipelsky and Chemelli does not teach or suggest such features. As discussed previously, it is respectfully submitted that the one-way check valves taught by Schnipelsky are not valves that are “closed by contact with the sample.” Rather, Schnipelsky teaches that fluid is allowed to pass through the valves when that fluid is in contact with those valves. According to Schnipelsky, it is only when the fluid backwashes do the valves close. [see Schnipelsky, column 10, lines 42-45; column 14, lines 42-48] *At most*, Chemelli teaches that each of the passageways is temporarily sealed. [see Chemelli, column 3, lines 8-23] It is respectfully submitted that **no** valve mechanism is taught or suggested by Chemelli. In addition, the combination of Schnipelsky and Chemelli is **improper**.

4. Rejection Of Claims 4 And 9 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Chemelli, And In Further View Of Zelin.

These claims recite the feature of at least one sensor capable of detecting an air-liquid interface, and in which the at least one sensor can comprise a conductimetric sensor. However, as discussed previously, neither Schnipelsky nor Chemelli teach or suggest the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the

sample. The combination of Schnipelsky, Chemelli, and Zelin does not teach or suggest such features. *At most*, Zelin teaches a sensing device 10 that includes an array of sensor elements 70 and several cavities 18, 20, 22, and conduits 220, 224, 228, and 234 that enable the test fluid sample collection, provide active reagents, calibrate the sensors, and enable the measurement by transporting fluids to and from the sensor elements 70. [see Zelin, column 7, 11-16] It is respectfully submitted that nowhere does Zelin teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky, Chemelli, and Zelin is **improper**.

5. Rejection Of Claims 10 And 11 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Opalsky.

These claims recite the feature in which the cartridge comprises a metering means for delivering a metered amount of the sample to the at least one analyte sensor, and the metering means can comprise a capillary stop within the first conduit. However, as discussed previously, Schnipelsky does not teach or suggest the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky and Opalsky does not teach or suggest such features. *At most*, Opalsky teaches a cartridge or housing 10 that includes a sample entry port 12 that allows introduction of a sample into the housing 10, and is surrounded by a circumferential excess sample well 14. Fluidically connected to the sample entry port 12, at one end, is a sample holding chamber or sample retaining area 20. Located at the other end of the sample retaining area 20 is a capillary stop 22. [see Opalsky, column 7, lines 56-65] According to Opalsky, a pre-sensor channel 24 leads from the capillary stop 22 to an analysis location 31. A waste tube 34 is also in communication with the analysis location 31. [see Opalsky, column 7, line 66 – column 8, line 12] It is respectfully submitted that nowhere does Opalsky teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky and Opalsky is **improper**.

6. Rejection Of Claim 13 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Wozniak.

This claim recites the feature that the closeable valve is selected from the group consisting of a dry sponge material coated with a fluid impermeable layer, a flap capable of blocking the valve and held open by a dry soluble compound, and a gelling polymer. However, as discussed previously, Schnipelsky does not teach or suggest the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky and Wozniak does not teach or suggest such features. As illustrated in Figure 1 of Wozniak, a hydrophilic expansion plug 18 is placed in the flow channel between a variable volume chamber 14 and a needle 16 in a self-annulling syringe. According to Wozniak, “[t]he syringe is used in a normal fashion to draw medication from a vial and inject it into the patient. However, after a short period of time the hydrophilic plug absorbs water from the residual in the syringe and swells to occlude the nozzle and render the syringe inoperable.” [Wozniak, column 3, lines 48-52 (emphasis added)] Thus, Wozniak teaches that the hydrophilic expansion plug is configured to allow fluid to be draw into and expelled from the syringe before the syringe becomes inoperative. It is only after a tailored expansion lapse time that the plug expands and blocks further fluid movement. [*see also* Wozniak, column 4, lines 26-34; column 4, line 67-column 5, line 3] It is respectfully submitted that nowhere does Wozniak teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky and Wozniak is **improper**.

7. Rejection Of Claims 15 And 16 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of McNeely.

These claims recite the feature that the second conduit comprises a valve responsive to hydrostatic pressure. However, as discussed previously, Schnipelsky does not teach or suggest

the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky and McNeely does not teach or suggest such features. McNeely merely teaches the use of stopping means or passive “valves” created by suitable pressure barriers to “impede the flow of fluids under certain conditions thereby allowing control of the fluid.” In particular, although these passive “valves” may regulate fluid flow, McNeely expressly teaches that the passive valves “do not move.” [see McNeely, column 5, lines 18-28] Rather, the passive “valves” are merely pressure barriers that impede the flow of fluid until sufficient pressure in the fluid has been reached to allow the fluid to push past such stopping means. [see McNeely, column 6, lines 43-46] Accordingly, it is respectfully submitted that nowhere does McNeely teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample.** In addition, the combination of Schnipelsky and McNeely is **improper.**

8. Rejection Of Claim 20 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Cathey.

This claim recites the feature that a portion of at least one conduit comprises at least one dry agent capable of dissolving in the fluid or sample. However, as discussed previously, Schnipelsky does not teach or suggest the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky and Chathey does not teach or suggest such features. According to Cathey, “[t]he control capillary is designed so that capillary flow in the control capillary is not impeded at the intersection with the flow path. However, capillary flow in the flow path is **impeded** at the intersection when the control capillary is **void of liquid** because of the sharp interruption in the depth of the flow path. Only when the control capillary is **full** is capillary flow in the intersected flow path **not** impeded.” [Cathey, column 5, lines 50-56 (emphasis added)] Thus, it is respectfully submitted that Cathey teaches that the capillary valves operate in a manner that is **opposite** to the valve recited in dependent claim 20. More particularly, the capillary valve taught

by Cathey impedes (“closes”) the flow of liquid when the control capillary is empty, and permits (“opens”) the flow of fluid when the control capillary is full. Accordingly, it is respectfully submitted that nowhere does Cathey teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky and Cathey is **improper**.

9. Rejection Of Claims 21-26, 28, 29, 32, And 33 Under 35 U.S.C. § 103(a)
As Allegedly Being Unpatentable Over Schnipelsky In View Of Cathey,
And In Further View Of Zier And Pourahmadi.

These claims recite the features of, for example: that the at least one dry reagent comprises an antibody-enzyme conjugate, a substrate for the antibody-enzyme conjugate, or a blocking agent; the at least one analyte sensor comprises an immunosensor; the fluid comprises a substrate for an antibody-enzyme conjugate; the at least one analyte sensor comprises an amperometric sensor, a potentiometric sensor, or a reference sensor; the cartridge comprises one or more mechanical or electrical connections for insertion of the cartridge into a reading apparatus; and the cartridge comprises an enzyme and a substrate capable of regenerating a product consumed by contact with the at least one analyte sensor, whereby a signal from the sensor is increased. However, as discussed previously, neither Schnipelsky nor Cathey teaches or suggests the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky, Cathey, Zier, and Pourahmadi does not teach or suggest such features. As illustrated in Figures 1-3 of Zier, the implantable electrochemical enzyme sensors 1 comprise a thin cylindrical tube-shaped cannula 10 made of metal that contains an insulating epoxy resin filler 12, as well as one or two axially directed measurement electrodes 14, 14'. The metallic tube jacket forms at the same time the reference electrode 11' of the electrochemical sensor. [see Zier, column 6, lines 58-66] It is respectfully submitted that Zier does not teach or suggest any type of valve or other like mechanism for use in or by the sensors. *At most*, Pourahmadi teaches that valves can act as “flow controllers” to divert the motion of fluid in the cartridge 101. [see Pourahmadi, page 4,

paragraph 0052] For example, the valves can be activated by magnetic forces to control the fluid motion. [see Pourahmadi, page 10, paragraph 0121] Accordingly, it is respectfully submitted that nowhere does Zier or Pourahmadi teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky, Cathey, Zier, and Pourahmadi is **improper**.

10. Rejection Of Claim 27 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Cathey, In View Of Zier, In View Of Pourahmadi, And Further In View Of Grundig.

This claim recites the feature that the substrate comprises a ferrocene or p-aminophenol phosphate. However, as discussed previously, neither Schnipelsky, Cathey, Zier, nor Pourahmadi teaches or suggests the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig does not teach or suggest such features. As illustrated in, for example, Figures 1 and 2 of Grundig, the invention relates to an enzymatic-electrochemical affinity sensor and a one-step affinity assay for the quantitative determination of analytes in aqueous media. [see Grundig, abstract] It is respectfully submitted that nowhere does Grundig teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig is **improper**.

11. Rejection Of Claims 31 And 36 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Pourahmadi.

These claims recite the features of the cartridge comprising a surface coating that decreases non-specific binding of a substance therein. These claims also recite the feature of the cartridge comprising a filter element interposed between the sample holding chamber and the at least one analyte sensor, and adjacent the at least one sensor, whereby the microparticles are

concentrated adjacent the at least one sensor. However, as discussed previously, neither Schnipelsky nor Pourahmadi teaches or suggests the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky and Pourahmadi is **improper**.

12. Rejection Of Claim 35 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Nelson.

This claim recites the feature that the microparticles are magnetic, and the means for localizing the microparticles is a magnet field. However, as discussed previously, Schnipelsky does not teach or suggest the feature of a valve connected to an opening in the first conduit, in which the valve is closed by contact with the sample. The combination of Schnipelsky and Nelson does not teach or suggest such features. According to Nelson, “[t]o control bulk fluid flow through the enrichment channel, e.g., to prevent waste sample from flowing into the main electrophoretic flowpath, fluid control means, e.g., valves, membranes, etc., may be associated with each of the inlets and outlets.” [Nelson, column 8, lines 52-56] In particular, as illustrated in Figure 1, “[f]or controlling fluid flow through the channel inlets and outlets, valves 8, 9 and 11 are provided.” [Nelson, column 12, lines 5-6] “Valves 8 and 9 are closed to prevent sample from flowing or ‘bleeding’ out inlet 4 or outlet 5. After the sample has flowed through channel 10, valve 11 is shut and valves 8 and 9 are opened.” [Nelson, column 12, lines 14-17] Thus, *at most*, it is respectfully submitted that Nelson teaches that the valves 8, 9, and 11 can act as “flow controllers” to control bulk fluid flow by suitably opening and closing. However, it is respectfully submitted that nowhere does Nelson teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**. In addition, the combination of Schnipelsky and Nelson is **improper**.

B. Objection To Claims 46 And 47, Because The Status Identifiers For These Claims Are Allegedly Unclear.

Contrary to the assertions of the Patent Office, it is respectfully submitted that the status identifiers associated with claims 46 and 47 are clear. However, to resolve any possible confusion on the part of the Patent Office, Appellants respectfully note that claims 46 and 47 are canceled.

C. Rejection Of Claims 2, 5, 14, 17-19, 30, 34, And 56 Under 35 U.S.C. § 102(b) As Allegedly Being Anticipated By Schnipelsky.

It is respectfully submitted that Schnipelsky does not teach at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in independent claim 2 of the present application.

a. The Schnipelsky Patent.

As understood by Appellants, Schnipelsky is directed to a cuvette and a method of use that prevent nucleic acid amplified by PCR technology from being released to the atmosphere, while still proceeding to a detection step to determine whether or not the nucleic acid is present. Detection reagents are either pre-incorporated into compartments in the cuvette or added after amplification. In the latter case, a check valve prevents amplified nucleic acid from being released. Transfer of liquids between compartments is achieved via the use of flexible compartment walls and an external pressure source, or via pistons that are part of the cuvette and operate on the compartments as a piston within a piston chamber. [see Schnipelsky, abstract]

More particularly, as illustrated in Figure 1, the cuvette 10 can feature flexible compartments that cooperate with an external pressurizing means 60, such as a pressure roller, to provide the total apparatus of the invention. [see Schnipelsky, column 9, lines 63-66] As taught by Schnipelsky, the compartments include a reaction compartment 26. Compartment 30 is a storage compartment for the first wash compartment. Compartment 32 is a storage compartment containing at least one of the detection materials pre-incorporated therein. Storage compartment 34 is a second wash-containing storage compartment. Storage compartment 36 has the remaining detection reagents pre-incorporated therein. Storage compartment 38 has pre-incorporated therein a stop solution to prevent too much leuco dye from converting to the dye. Compartment 40 is the detection site, and compartment 42 is the waste compartment. Compartment 42 connects to compartment 40 via passageway 43. According to Schnipelsky, a

one-way check valve can be included in passageway 43 “to prevent waste liquid from backwashing into compartment 40, thus creating undesirable background color.” [Schnipelsky, column 10, lines 13-45]

As further illustrated in Figure 1, the interconnections of the cuvette 10 are as follows. Passageway 21 connects injection aperture 22 with compartment 26. Passageway 44 connects reaction compartment 26 with detection compartment 40. Passageway 48 connects compartment 30, passageway 49 connects compartment 32, passageway 50 connects compartment 34, passageway 52 connects compartment 36, and passageway 54 connects compartment 38, all with detection compartment 40. Passageway 54 serves as the trunk line to which the others (48, 49, 50 and 52) are joined. [see Schnipelsky, column 10, lines 46-61]

- b. The Schnipelsky Patent Does Not Teach At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Independent Claim 2 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Schnipelsky does not teach at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, independent claim 2 of the present application.

As understood by Appellants, and as illustrated in Figure 1, Schnipelsky teaches that “a one-way check valve (not shown) can be included in passageway [43]² to prevent waste liquid from backwashing into compartment 40, thus creating undesirable background color.”

² The original sentence in the Schnipelsky patent indicates that the one-way check valve can be included in “passageway 44” to prevent waste liquid from backwashing into compartment 40. However, compartment 42 is the waste compartment, and “[c]ompartiment 42 connects to compartment 40 via passageway 43.” [Schnipelsky, column 10, lines 38-46 (emphasis added)] If the one-way check valve was placed in passageway 44 and not passageway 43, there would be no structure or other mechanism to prevent the waste liquid from backwashing from waste compartment 42 into detection compartment 40 and “creating an undesirable background color.” Therefore, it is respectfully submitted that Schnipelsky contains an easily-identifiable typographical error with respect to the numeral used to reference the passageway discussed in this sentence.

[Schnipelsky, column 10, lines 42-45 (emphasis added)] According to an alternative embodiment illustrated in Figure 7,

a check valve 80 can be inserted into passageway 54B to prevent a backwash of DNA into those compartments [(i.e., compartments 30B, 32B, 34B, 36B, 38B, 40B, and 42B)]. Such a valve is conventional, and can comprise, for example, FIG. 8, a seat 82, and a ball 84 which, when pushed back upstream, seats on seat 82 to stop flow. Ball 84 is free, however, to flow downstream up against a small stop 86. [Schnipelsky, column 14, lines 42-48 (emphasis added)]

In other words, the one-way check valve for the embodiment illustrated in Figure 1 and the check valve 80 for the embodiment illustrated in Figure 7 each allow fluid to travel in one direction (i.e., downstream) and remain open when the fluid travels in the given direction, but prevent a backwash of liquid from traveling in the opposite direction (i.e., upstream).

Thus, Schnipelsky teaches that fluid is allowed to pass through the valves when that fluid is in contact with those valves. According to Schnipelsky, it is only when the fluid backwashes do the one-way check valves close. Such a manner of operation of these valves is a requirement of Schnipelsky: “there must be provided means such as one-way check valves that allow such storage compartments to feed reagent to the amplified nucleic acid, but not amplified nucleic acid to the storage compartments.” [Schnipelsky, column 9, lines 40-46 (emphasis added)] Such a manner of operation of these check valves is wholly different than the valve recited in independent claim 2 of the present application.

In complete contrast to Schnipelsky, the valve recited in independent claim 2 of the present application is “**closed by contact with said sample.**” As discussed previously, such a valve can be comprised of a dried sponge material or the like that is coated with an impermeable substance. As illustrated in Figures 4 and 5 of the present application, contacting the sponge material with the sample or a fluid results in swelling of the sponge to fill the cavity, thereby substantially blocking further flow of liquid into the waste chamber. Furthermore, sealing of the opening to the waste chamber upon wetting of the closeable valve provides an airtight seal that blocks the flow of air between the first conduit and the waste chamber to permit the first pump connected to the sample chamber to displace fluid within the second conduit (e.g.,

to allow fluid in the second conduit to be drawn in contact with the sensor). [see present application, page 15, lines 11-18] There are several different design examples for such a valve that are encompassed within the present invention. Some designs are activated mechanically while others activate on liquid contact. Other types of closeable valves that are encompassed by the present invention include, but are not limited to: a flexible flap held in an open position by a soluble glue or a gelling polymer that dissolves or swells upon contact with a fluid or sample thus causing the flap to close; and, alternatively, a thin layer of a porous paper or similar material interposed between a conduit and either the waste chamber or ambient air such that the paper is permeable to air while dry but impermeable when wet. [see present application, page 15, line 25-page 16, line 13]

The error in the Patent Office's reading of Schnipelsky is clearly evident if the valve recited in independent claim 2 is substituted for the check valves taught by Schnipelsky. For example, assume that the valve recited in independent claim 2 is substituted for the one-way check valve in passageway 43 of Figure 1 of Schnipelsky. Upon contact with the waste liquid from detection compartment 40, the (substituted) valve closes. Thereafter, waste liquid is prevented from entering the waste compartment 42. Instead, all waste liquid backwashes into detection compartment 40, "thus creating undesirable background color." [Schnipelsky, column 10, lines 42-46] The valve recited in independent claim 2 of the present application would create the "undesirable" situation that the one-way check valve used by Schnipelsky is designed to prevent. In other words, the valve recited in independent claim 2 would at least detrimentally affect the operation of the cuvette 10 taught by Schnipelsky, if not render the cuvette 10 unusable. Accordingly, the manner of operation of the check valves taught by Schnipelsky is different than the valve recited in independent claim 2.

It is a fundamental tenet of the patent laws regarding anticipation that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." [M.P.E.P. § 2131 (emphasis added)] In other words, "[t]he identical invention must be shown in as complete detail as is contained in the . . . claim." [M.P.E.P. § 2131 (citations omitted) (emphasis added)] It is respectfully submitted

that Schnipelsky does not teach that either the one-way check valve or check valve 80 are “closed by contact with said sample.” It is further respectfully noted the Patent Office has not provided a citation to any passage in Schnipelsky that teaches such a feature. Rather, *at most*, the Patent Office states that Schnipelsky teaches that the “check valve closes upon contact with sample moving back through the conduit . . .” [Final Office Action, page 3, lines 2-3 (emphasis added); *see also* page 11, lines 18-19] It is respectfully submitted that no such highlighted language is recited in independent claim 2 of the present application. Rather, it is respectfully submitted that the Patent Office is impermissibly attempting to read unrecited limitations into the claim. As the manner of operation of the one-way check valve taught by Schnipelsky is different than the valve recited in independent claim 2 of the present application, it is respectfully submitted that Schnipelsky does not anticipate the subject matter of independent claim 2.

In addition, “[t]he elements [in the reference] must be arranged as required by the claim . . .” [M.P.E.P. § 2131 (citations omitted)] For example, independent claim 2 recites the feature of “a first conduit connected to said sample holding chamber,” and “a second conduit for retaining a fluid, said second conduit connected to said first conduit.” However, the Patent Office asserts that “channels 44, 54, **and** 40 comprise a first conduit . . .” [Final Office Action, page 2, lines 18-19 (emphasis added)] Initially, it is noted that Schnipelsky teaches that 44 and 54 are passageways, and 40 is the detection compartment. Additionally, it is respectfully submitted that passageways 44 and 54 are separate and distinct from each other and from the detection compartment 40. As noted previously, passageway 44 connects reaction compartment 26 with detection compartment 40, and passageway 54 connects storage compartment 38 with detection compartment 40. [*see* Schnipelsky, column 10, lines 46-57] However, “[t]he compartments are deliberately positioned . . . so that each one will empty into compartment 40 in the proper sequence as roller 60 advances along path A in the direction of arrows 63.” [Schnipelsky, column 10, lines 62-65 (emphasis added)] Each passageway is blocked off with pinch points P₁-P₅ as each compartment is emptied so that a liquid, when ejected from its compartment, will not backwash up the passageway used to empty another compartment that is further downstream. [*see* Schnipelsky, column 11, lines 37-30] As taught by Schnipelsky,

if pressure is applied to all of P₁ -P₅ to close off the exit passageways except for passageway 44, pressure can be simultaneously applied (by, e.g., appropriately placed air pistons) to all of compartments 26, 30, 32, 34, 36 and 38. However, since only passageway 44 is unblocked, only the amplified DNA will transfer. Thereafter, pinch point P₁ only, is released, allowing transfer of wash liquid out through passageway 49, and so forth until pinch point P₅ is finally released.

[Schnipelsky, column 12, lines 22-32]

Thus, each of the passageways 44, 48, 49, 50, 52, and 54 illustrated in Figure 1 are separate and distinct from each other. Fluid from one passageway is prevented from backwashing or otherwise flowing up another passageway as the fluid is released from each compartment through each corresponding passageway in sequence. In addition, each passageway is separate and distinct from each compartment, as the passageways are merely used to individually connect compartments 26, 30, 32, 34, 36, and 38, respectively, to the detection compartment 40. Despite the express teachings of Schnipelsky, it is respectfully submitted that the Patent Office is casually re-arranging the features taught by Schnipelsky at its discretion in an attempt to anticipate the claims of the present application.

As discussed previously, Schnipelsky does not teach an “identical” invention as is recited in independent claim 2. For example, the Patent Office acknowledges that Schnipelsky “do[es] not specifically teach a second conduit capable of fluid retention.” [Final Office Action, page 3, lines 7-9] Additionally, the Patent Office has failed to show that Schnipelsky teaches elements that are arranged as required by independent claim 2. A tortured and contorted interpretation of the features recited in independent claim 2 and a tortured and contorted reading of Schnipelsky cannot replace the mandates and requirements of the patent laws regarding anticipation. It is respectfully submitted that the Patent Office has utterly failed to meet the established requirements of anticipation with respect to independent claim 2.

Furthermore, although the Patent Office admits that Schnipelsky does not teach the feature of a second conduit for retaining a fluid, as recited in independent claim 2, the Patent Office asserts that “the conduit does not appear to require any further properties to retain fluid, and therefore the conduit of Schnipelsky et al. would be capable of retaining fluid.” [Final Office

Action, page 3, lines 7-9] According to the established requirements of anticipation, “[t]he identical invention must be shown in as complete detail as is contained in the . . . claim.” [M.P.E.P. § 2131 (citations omitted) (emphasis added)] It is respectfully submitted that merely pointing out what a reference may teach, without showing where each and every element of the identical invention is actually taught in the reference, is in no way sufficient to meet the established requirements of anticipation.

Regarding the Patent Office’s assertion, according to M.P.E.P. § 2112, “[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.” [(citations omitted, emphasis in original)] More particularly,

[t]o establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [M.P.E.P. § 2112 (citations omitted) (emphasis added)]

“In relying upon the theory of inherency, the examiner *must* provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.” [M.P.E.P. § 2112 (emphasis added and in original)] Accordingly, Appellants respectfully traverse such an assertion of inherency and request that the Patent Office cite a document in support of this determination so that the Appellants have a full and fair opportunity to respond to the combination of documents.

In sum, it is respectfully submitted that Schnipelsky does not teach numerous features of the present invention, as recited in, for example, independent claim 2. The Patent Office has utterly failed to identify in Schnipelsky where “[t]he identical invention [is] shown in as complete detail as is contained in the . . . claim.” It is respectfully submitted that the Patent Office has completely failed to meet the established requirements of anticipation with respect to independent claim 2.

- c. Since Schnipelsky Does Not Teach At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Independent Claim 2 Of The Present Application, Schnipelsky Does Not Anticipate Independent Claim 2.

Since Schnipelsky does not teach at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, it is respectfully submitted that the Schnipelsky does not anticipate independent claim 2.

Dependent claims 5, 14, 17-19, 30, 34, and 56 variously depend from independent claim 2, and are, therefore, patentably distinguishable over Schnipelsky for at least those reasons stated above with regard to independent claim 2.

For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not anticipate the subject matter of claims 2, 5, 14, 17-19, 30, 34, and 56.

Hence, the subject matter of claims 2, 5, 14, 17-19, 30, 34, and 56 is separately patentable for this reason.

D. Rejection Of Claims 3, 6-8, And 12 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Chemelli.

It is respectfully submitted that the combination of Schnipelsky and Chemelli is improper. *Even if* the combination of Schnipelsky and Chemelli was proper, it is respectfully submitted that Schnipelsky and Chemelli, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in independent claim 3 of the present application.

a. The Chemelli Patent.

As understood by Appellants, Chemelli is directed to a method for forcing liquid out of a burstable compartment into a detection chamber without also forcing residual air of that compartment to interfere with liquid detection. According to Chemelli, the method features the step of i.) applying pressure sufficient to eject the liquid but not the residual air, ii.) retaining that pressure as long as the reaction period of the liquid takes place, called the incubation period, and iii.) completing the ejection to eject residual air into the chamber. [see Chemelli, abstract]

b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Independent Claim 3 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, independent claim 3 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of independent claim 3 obvious.

- c. The Chemelli Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Independent Claim 3 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Chemelli does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, independent claim 3 of the present application.

As illustrated in Figure 1 of Chemelli, a reaction cuvette 10 includes an inlet port 22 for patient injection of sample liquid, which connects via a passageway 21 to a PCR reaction compartment 26. A seal 46 temporarily blocks flow out of compartment 26. When seal 46 is broken, liquid feeds via a passageway 44 to a detection chamber 40 having detection sites 41. The reaction cuvette 10 also include additional compartments 30, 32, 34, and, optionally, additional compartment 36, each feeding via passageways 48, 50, and 52, to chamber 40. Each of those passageways is temporarily sealed at 56, and contains an appropriate reagent liquid. [see Chemelli, column 3, lines 8-23] Compartment 42 is a waste-collecting compartment. [see Chemelli, column 3, line 59]

It is respectfully submitted that nowhere does Chemelli teach or even suggest the feature of a valve connected to an opening in the first conduit, in particular, a valve that is closed by contact with the sample. *At most*, Chemelli teaches that each of the passageways is temporarily sealed (at 46 or 56). For example, unlike Schnipelsky, it is respectfully noted that Chemelli does not even teach or suggest that a valve or other mechanism is located between the detection chamber 40 and the waste-collecting compartment 42 to prevent backwashing of waste liquid into the detection compartment 40.

The Appellants respectfully note that the Patent Office has failed to indicate where in Chemelli the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Chemelli does not address the above-identified deficiencies of Schnipelsky.

- d. Since the Combination of Schnipelsky and Chemelli Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Independent Claim 3 Of The Present Application, The Combination Of Schnipelsky And Chemelli Does Not Render Independent Claim 3 Obvious.

Since Schnipelsky and Chemelli, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, independent claim 3 of the present application, it is respectfully submitted that the combination of Schnipelsky and Chemelli does not render independent claim 3 unpatentable.

In addition, according to M.P.E.P. § 2143, to establish a prima facie case of obviousness, three basic criteria must be met. “First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.” [M.P.E.P. § 2143] In other words, “[o]bviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art.” [M.P.E.P. § 2143.01] “The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved.” [*In re Kotzab*, 217 F.3d 1365, 1370, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000)] The showing must be “clear and particular, and it must be supported by **actual evidence**.” [*Teleflex, Inc. v. Ficosa North American Corp.*, 299 F.3d 1313, 1334, 63 U.S.P.Q.2d 1374, 1387 (Fed. Cir. 2002) (quoting *In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999))

(emphasis added)] It is not sufficient to rely on “common sense and common knowledge,” as there must be specific evidence to support the motivation. [see *In re Lee*, 277 F.3d. 1338, 1344-45, 61 U.S.P.Q.2d 1430, 1434-35 (Fed. Cir. 2002)]

With regard to the combination of Schnipelsky and Chemelli, the Patent Office asserts that “[i]t would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al., means for inserting at least one air segment into the first or second conduit as taught by Chemelli, in order to prevent interference of air pockets or bubbles with the detection chamber.” [Final Office Action, page 4, lines 19-22] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky, Chemelli, or any other source, to support such an unfounded and baseless assertion.

It is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky and Chemelli is merely a bald assertion wholly and completely without support in either Schnipelsky or Chemelli. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness.

Rather, according to M.P.E.P. § 2142, “[t]o reach a proper determination under 35 U.S.C. 103, . . . impermissible hindsight must be avoided and the legal conclusion [of obviousness] must be reached on the basis of the facts gleaned from the prior art.” Furthermore, according to M.P.E.P. § 2143.01, “[t]he mere fact that references can be . . . modified does not render the resultant combination obvious unless the prior art also suggests the desirability of [such

modification].” [citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990)] It is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky and Chemelli is wholly and completely without support, either explicitly or implicitly. It is respectfully submitted that the Patent Office’s attempt to combine Schnipelsky and Chemelli for its rejection based on obviousness is clearly and unequivocally founded upon “knowledge gleaned only from applicant’s disclosure.” [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and Chemelli does not render the subject matter of independent claim 3 obvious.

Dependent claims 6-8, and 12 variously depend from independent claim 3, and are, therefore, patentably distinguishable over the combination of Schnipelsky and Chemelli for at least those reasons stated above with regard to independent claim 3.

For at least the foregoing reasons, it is respectfully submitted that the combination of Schnipelsky and Chemelli does not render the subject matter of claims 3, 6-8, and 12 unpatentable.

Hence, the subject matter of claims 3, 6-8, and 12 is separately patentable for this reason.

E. Rejection Of Claims 4 And 9 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Chemelli, And In Further View Of Zelin.

It is respectfully submitted that the combination of Schnipelsky, Chemelli, and Zelin is improper. *Even if* the combination of Schnipelsky, Chemelli, and Zelin was proper, it is respectfully submitted that Schnipelsky, Chemelli, and Zelin, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 4 of the present application.

a. The Zelin Patent.

As understood by Appellants, Zelin is directed to a method for automatic fluid flow compensation in disposable fluid analysis sensing devices. The method is designed to keep the test conditions from sample to sample substantially unchanged. This is accomplished by using information about the preceding and/or current test measurements to automatically offset parameter variations of the disposable devices and the reading apparatus caused by manufacturing tolerances, wear of the mechanical parts, fluid viscosity differences and others. At each consecutive test measurement, the method uses a compensation of the position of the actuating element to offset the difference between the previous test measurement and a factory pre-specified value. The method and system result, over the lifetime of the instrument, in a substantially unchanged flow of the analyzed fluid and reduction of the influence of a variety of external factors on the test measurements. [see Zelin, abstract]

- b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 4 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 4 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 4 obvious.

- c. The Chemelli Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 4 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(D)(c) of the present Appeal Brief, it is respectfully submitted that Chemelli does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 4 of the present application.

Consequently, it is respectfully submitted that Chemelli does not address the above-identified deficiencies of Schnipelsky.

- d. The Zelin Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 4 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Zelin does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in

which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 4 of the present application.

As illustrated in Figure 2 of Zelin, a sensing device 10 includes an array of sensor elements 70 and several cavities 18, 20, 22 and conduits 220, 224, 228, and 234 that enable the test fluid sample collection, provide active reagents, calibrate the sensors, and enable the measurement by transporting fluids to and from the sensor elements 70. [see Zelin, column 7, 11-16] As illustrated in Figures 2 and 4, a first cavity 18 is located in the center of the device 10 that has a pin 40 at its bottom, a hinged disk 102 at the top, and a first conduit 220 that leads from cavity 18. A sealed pouch 60 containing fluid adapted to calibrate the sensor elements 70 resides in the cavity 18. A second conduit 224 includes an orifice at one end for the receipt of a test fluid sample, while the other end terminates at a capillary break 222. A third conduit 228 leads from the capillary break 222 past the sensor elements 70 to a second cavity 20 that serves as a sink. The first conduit 220 enters the third conduit 228 between the capillary break 222 and the sensor array 70. A third cavity 22 serves as an air bladder 229. When the air bladder 229 is depressed, air is forced down a fourth conduit 234 into the second conduit 224 displacing in the process the fluids within the sensing device. [see Zelin, column 7, lines 17-31] However, it is respectfully submitted that nowhere does Zelin teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**.

The Appellants respectfully note that the Patent Office has failed to indicate where in Zelin the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Zelin does not address the above-identified deficiencies of Schnipelsky and Chemelli.

- e. Since the Combination of Schnipelsky, Chemelli, and Zelin Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 4 Of The Present Application, The Combination Of Schnipelsky, Chemelli, and Zelin Does Not Render Dependent Claim 4 Obvious.

Since Schnipelsky, Chemelli, and Zelin, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 4 of the present application, it is respectfully submitted that the combination of Schnipelsky, Chemelli, and Zelin does not render dependent claim 4 unpatentable.

With regard to the combination of Schnipelsky, Chemelli, and Zelin, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al. in view of Chemelli, a conductivity sensor as taught by Zelin, in order to increase the consistency and reliability of the output measurement by ensuring that all air is out of the detection chamber while liquid reactions are taking place.” [Final Office Action, page 5, lines 12-16] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky, Chemelli, Zelin, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky, Chemelli, and Zelin is a bald assertion wholly and completely without support in either Schnipelsky, Chemelli, or Zelin. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or

motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office's attempt to combine Schnipelsky, Chemelli, and Zelin for its rejection based on obviousness is clearly and unequivocally founded upon "knowledge gleaned only from applicant's disclosure." [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky, Chemelli, and Zelin does not render the subject matter of dependent claim 4 obvious.

Dependent claim 9 depends from claim 4, and is, therefore, patentably distinguishable over the combination of Schnipelsky, Chemelli, and Zelin for at least those reasons stated above with regard to dependent claim 4.

For at least the foregoing reasons, it is respectfully submitted that the combination of Schnipelsky, Chemelli, and Zelin does not render the subject matter of claims 4 and 9 unpatentable.

Hence, the subject matter of claims 4 and 9 is separately patentable for this reason.

F. Rejection Of Claims 10 And 11 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Opalsky.

It is respectfully submitted that the combination of Schnipelsky and Opalsky is improper. *Even if* the combination of Schnipelsky and Opalsky was proper, it is respectfully submitted that Schnipelsky and Opalsky, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 10 of the present application.

a. The Opalsky Patent.

As understood by Appellants, Opalsky is directed to a sample analyzing system that includes at least one sensor located at least partially within a sample retaining area. In addition, the sensor has at least one edge defining a sample detection location. The sample detection location defines an area within which the sensor is capable of detecting the presence or absence of the sample. According to Opalsky, the system analyzes sample data by first introducing the sample into the sample retaining area and then mixing a reagent with the sample to commence formation of a reagent product. After mixing and upon detecting the absence of the sample from the sample detection location by the at least one sensor, an edge of the sample is moved past an edge of the at least one sensor and into the sample detection location. Then, upon detecting the presence of the sample in the sample detection location by the at least one sensor, the edge of the sample is moved past the edge of the at least one sensor and out of the sample detection location. Additionally, between oscillations, data may be collected by one or more sensors. By repeating these steps, an accumulation of material on or about the at least one sensor can be prevented. [see Opalsky, abstract]

- b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 10 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 10 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 10 obvious.

- c. The Opalsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 10 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Opalsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 10 of the present application.

As illustrated in Figure 1 of Opalsky, a cartridge or housing 10 includes a sample entry port 12 that allows introduction of a sample into the housing 10, and is surrounded by a circumferential excess sample well 14. A snap cover 38 encloses the sample entry port 12 with the formation of an air-tight seal. Fluidically connected to the sample entry port 12, at one end, is a sample holding chamber or sample retaining area 20. Located at the other end of the sample retaining area 20 is a capillary stop 22. [see Opalsky, column 7, lines 56-65] According to Opalsky, a pre-sensor channel 24 leads from the capillary stop 22 to an analysis location 31. In addition, a hydrophobic layer 26 is positioned between the pre-sensor channel 24 and the analysis location 31. A reagent and/or a substrate 30 can be deposited or introduced into the

system at analysis location 31. Although the reagent 30 is depicted as being downstream of sensors 28 and 29, it is possible to position the reagent 30 upstream of sensors 28 and 29 so that a sample passes through the reagent 30 before reaching the sensors. Furthermore, in communication with the analysis location 31 are one or more conductimetric sensors 28, one or more amperometric sensors 29, and one or more reference sensors 32. A waste tube 34 is also in communication with the analysis location 31. [see Opalsky, column 7, line 66 – column 8, line 12] A sample can be moved within the system through use of a flexible diaphragm pump 36. The pump 36 facilitates movement of the sample by pumping air through the air tube 18, through overflow chamber 16, and finally into sample retaining area 20. [see Opalsky, column 8, lines 13-17]

However, it is respectfully submitted that nowhere does Opalsky teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample.**

The Appellants respectfully note that the Patent Office has failed to indicate where in Opalsky the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Opalsky does not address the above-identified deficiencies of Schnipelsky.

- d. Since the Combination of Schnipelsky and Opalsky Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 10 Of The Present Application, The Combination Of Schnipelsky, and Opalsky Does Not Render Dependent Claim 10 Obvious.

Since Schnipelsky and Opalsky, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 10 of the present application, it is respectfully submitted that the combination of Schnipelsky and Opalsky does not render dependent claim 10 unpatentable.

With regard to the combination of Schnipelsky and Opalsky, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al., a means for metering as taught by Opalsky et al., in order to regulate the amount of volume entering the detection chamber.” [Final Office Action, page 6, lines 3-6] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky or Opalsky, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky and Opalsky is a bald assertion wholly and completely without support in either Schnipelsky or Opalsky. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office’s attempt to combine Schnipelsky and Opalsky for its rejection based on obviousness is clearly and unequivocally founded upon “knowledge gleaned only from applicant’s disclosure.” [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and Opalsky does not render the subject matter of dependent claim 10 obvious.

Dependent claim 11 depends from claim 10, and is, therefore, patentably distinguishable over the combination of Schnipelsky and Opalsky for at least those reasons stated above with regard to dependent claim 10.

For at least the foregoing reasons, it is respectfully submitted that the combination of Schnipelsky and Opalsky does not render the subject matter of claims 10 and 11 unpatentable. Hence, the subject matter of claims 10 and 11 is separately patentable for this reason.

G. Rejection Of Claim 13 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Wozniak.

It is respectfully submitted that the combination of Schnipelsky and Wozniak is improper. *Even if* the combination of Schnipelsky and Wozniak was proper, it is respectfully submitted that Schnipelsky and Wozniak, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 13 of the present application.

a. The Wozniak Patent.

As understood by Appellants, Wozniak is directed to a single-use, self-annulling syringe that is rendered inoperative after a single use without requiring any deliberate action on the part of a user. The injection device uses a hydrophilic expansion plug positioned in the outlet flow channel of the syringe, which expands a short time after being exposed to a drug containing water, thereby rendering the syringe inoperative. [see Wozniak, abstract]

b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 13 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 13 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 13 obvious.

- c. The Wozniak Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 13 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Wozniak does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 13 of the present application.

As illustrated in Figure 1 of Wozniak, a hydrophilic expansion plug 18 is placed in the flow channel between a variable volume chamber 14 and a needle 16 in a self-annulling syringe. According to Wozniak, “[t]he syringe is used in a normal fashion to draw medication from a vial and inject it into the patient. However, after a short period of time the hydrophilic plug absorbs water from the residual in the syringe and swells to occlude the nozzle and render the syringe inoperable.” [Wozniak, column 3, lines 48-52 (emphasis added)] “The period of time from introduction of liquid into the syringe to expansion of the hydrophilic plug, rendering the syringe inoperative, can range from 30 seconds to 30 minutes or larger, by choice of material for the hydrophilic plug.” [Wozniak, column 3, lines 53-57 (emphasis added)] According to an experimental example,

[t]he modified syringe was found to initially function normally with fluid being drawn into the piston and injected through the needle. The needle was then set aside for approximately 5 minutes and it was found that the syringe was no longer functional, demonstrating the self-annulling action. Since the full dose of fluid was expelled with the operation of the syringe, only the water residual in the syringe nozzle was needed to fully expand the PEO hydrophilic spiral. [Wozniak, column 4, lines 26-34 (emphasis added)]

In Figure 4, Wozniak illustrates a single-use self-annulling syringe pre-filled with a lyophilized drug. According to Wozniak, “[t]he syringe is . . . used to draw diluent, generally sterile water, into the syringe to reconstitute the vaccine in the syringe.” [Wozniak, column 4, lines 60-62] “The hydrophilic expansion plug has a tailored expansion lapse time to allow sufficient time for

the lyophilized drug to reconstitute with diluent and sufficient time for injection in the patient **before** self-annulling occurs.” [Wozniak, column 4, line 67-column 5, line 3]

Thus, Wozniak teaches that the hydrophilic expansion plug is configured to allow fluid to be draw into and expelled from the syringe before the syringe becomes inoperative. It is only after a tailored expansion lapse time that the plug expands and blocks further fluid movement. Such a manner of operation of the hydrophilic expansion plug is wholly different than the valve recited in dependent claim 13 of the present application.

In complete contrast to Wozniak, the valve recited in dependent claim 13 of the present application is “**closed by contact with said sample.**” As discussed previously, such a valve can be comprised of a dried sponge material or the like that is coated with an impermeable substance. As illustrated in Figures 4 and 5 of the present application, contacting the sponge material with the sample or a fluid results in swelling of the sponge to fill the cavity, thereby substantially blocking further flow of liquid into the waste chamber. [*see* present application, page 15, lines 11-18] As noted previously, there are several different design examples for such a valve that are encompassed within the present invention. Some designs are activated mechanically while others activate on liquid contact. [*see* present application, page 15, line 25-page 16, line 13]

The error in the Patent Office’s reading of Wozniak is clearly evident if the valve recited in dependent claim 13 is substituted for the hydrophilic expansion plug taught by Wozniak. For example, assume that the valve recited in dependent claim 13 is substituted for the hydrophilic expansion plug 18 in the flow channel between the variable volume chamber 14 and the needle 16 in the syringe illustrated in Figure 1 of Wozniak. Upon contact with the liquid (e.g., a medication drawn from a vial), the (substituted) valve closes. Thereafter, any and all liquid is prevented from being drawn into the syringe or expelled from the syringe. The syringe is thereby rendered inoperative before the fluid can be completely drawn into the syringe and before such fluid can be injected into a patient. In other words, the valve recited in dependent claim 13 would at least severely detrimentally affect the operation of the single-use, self-

annulling syringe taught by Wozniak, if not render the syringe completely unusable for its intended purpose.

For at least the foregoing reasons, it is respectfully submitted that nowhere does Wozniak teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**.

The Appellants respectfully note that the Patent Office has failed to indicate where in Wozniak the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Wozniak does not address the above-identified deficiencies of Schnipelsky.

- d. Since the Combination of Schnipelsky and Wozniak Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 13 Of The Present Application, The Combination Of Schnipelsky, and Wozniak Does Not Render Dependent Claim 13 Obvious.

Since Schnipelsky and Wozniak, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 10 of the present application, it is respectfully submitted that the combination of Schnipelsky and Wozniak does not render dependent claim 13 unpatentable.

With regard to the combination of Schnipelsky and Wozniak, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute for the one-way check valve of Schnipelsky et al., a gelling polymer closed by contact with the fluid sample as taught by Wozniak et al., in order to provide a low cost one-way valve that does not require mechanical components.” [Final Office Action, page 6, lines 3-6; *see also* page 13, lines 2-14] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an

alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky or Wozniak, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office's stated motivation for combining Schnipelsky and Wozniak is a bald assertion wholly and completely without support in either Schnipelsky or Wozniak. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office's stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office's attempt to combine Schnipelsky and Wozniak for its rejection based on obviousness is clearly and unequivocally founded upon "knowledge gleaned only from applicant's disclosure." [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

In addition, it is respectfully submitted that the Patent Office's comments describing the "gelling polymer" taught by Wozniak as a type of "low cost one-way valve" that can be substituted in Schnipelsky are baseless, unfounded, and in complete error. As described previously, Wozniak teaches that the hydrophilic expansion plug is configured to allow fluid to be drawn into and expelled from the syringe before the syringe becomes inoperative. After a tailored expansion lapse time, the plug expands and blocks further fluid movement. Accordingly, if the "gelling polymer" taught by Wozniak were used for the one-way check valve taught by Schnipelsky, waste liquid would be allowed to backwash into the detection compartment 40 during the "tailored expansion lapse time" before the "gelling polymer" expanded and closed off passageway 43 of cuvette 10 of Schnipelsky. In addition, after the "gelling polymer" expanded and closed off the passageway 43, all further waste liquid would be prevented from moving into the waste compartment 42. Instead, all such waste liquid would be

forced back or otherwise backwashed into the detection compartment 40. Either circumstance would create the “undesirable background color” that the one-way check valves of Schnipelsky are designed to prevent. [see Schnipelsky, column 10, lines 42-46] In other words, the “gelling polymer” taught by Wozniak would at least severely detrimentally affect the operation of the cuvette 10 taught by Schnipelsky, if not render the cuvette 10 unusable. It is for this additional reason that one of ordinary skill in the art would **not** be motivated to combine the teachings of Wozniak with the teachings of Schnipelsky. Rather, it is respectfully submitted that Wozniak teaches away from Schnipelsky in light of the properties and characteristics of Wozniak’s hydrophilic expansion plug. Additionally, according to M.P.E.P. § 2143.02, “[t]he prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success.” [(citations omitted)] For at least the foregoing reasons, it is respectfully submitted that the Patent Office has utterly failed to show that the “gelling polymer” taught by Wozniak would have a reasonable expectation of success in the cuvette 10 taught by Schnipelsky.

Furthermore, contrary to the assertions of the Patent Office, it is respectfully submitted that Wozniak is non-analogous art. According to M.P.E.P. § 2141.01(a), “[i]n order to rely on a reference as a basis for rejection of an applicant’s invention, the reference must either be in the field of applicant’s endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned.” [M.P.E.P. § 2141.01(a) (citations omitted)] Additionally, “[w]hile Patent Office classification of references and the cross-references in the official search notes of the class definitions are some evidence of ‘nonanalogy’ or ‘analogy’ respectively, the court has found ‘the similarities and differences in structure and function of the inventions to carry far greater weight.’” [M.P.E.P. § 2141.01(a) (citations omitted) (emphasis added)]

As discussed previously, Wozniak is directed to a single-use, self-annulling injection syringe for injecting a fluid into a patient. In complete contrast, exemplary embodiments of the present invention are directed to an apparatus and method for rapid *in situ* determinations of analytes in liquid samples that is capable of being used, for example, in the point-of-care clinical

diagnostic field. [*see* present application, page 1, lines 5-8] In other words, exemplary embodiments of the present invention are directed to an apparatus and its method of use for determining the presence and/or concentrations of analytes in a liquid sample. More particularly, the present invention provides single-use disposable cartridges adapted for conducting diverse real-time or near real-time assays of analytes. [*see* present application, page 1, lines 9-24]

Contrary to the assertions of the Patent Office, it is respectfully submitted that Wozniak is not within the field of Appellants' endeavor and not reasonably pertinent to the particular problem with which the Appellants were concerned. Additionally, it is respectfully submitted that the "structure and function" of the inventions of Wozniak and the present invention are utterly and completely dissimilar and different. Simply because "the references of Wozniak and Schnipelsky both teach techniques that prevent fluid from flowing in a certain direction in a fluidic device" is nowhere near sufficient support to consider two utterly disparate and different inventions as analogous art. [*see* Final Office Action, page 12, lines 12-14] Consequently, it is respectfully submitted that Wozniak is non-analogous art to the present invention, and, therefore, the Patent Office has improperly relied on Wozniak in its attempt to render the claims of the present application obvious.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and Wozniak does not render the subject matter of dependent claim 10 obvious.

Dependent claim 11 depends from claim 10, and is, therefore, patentably distinguishable over the combination of Schnipelsky and Wozniak for at least those reasons stated above with regard to dependent claim 10.

For at least the foregoing reasons, it is respectfully submitted that the combination of Schnipelsky and Wozniak does not render the subject matter of claims 10 and 11 unpatentable.

Hence, the subject matter of claims 10 and 11 is separately patentable for this reason.

H. Rejection Of Claims 15 And 16 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of McNeely.

It is respectfully submitted that the combination of Schnipelsky and McNeely is improper. *Even if* the combination of Schnipelsky and McNeely was proper, it is respectfully submitted that Schnipelsky and McNeely, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 15 of the present application.

a. The McNeely Patent.

As understood by Appellants, McNeely is directed to methods of controlling fluid flow through microchannels by use of passive valves or stopping means in the microchannels. The passive valves act as pressure barriers impeding flow of solution past the stopping means until enough force is built up to overcome the force of the pressure barrier. Well planned use of such stopping means acting as passive valves allows the flow of fluids through microchannels to be regulated so as to allow fluids to be mixed or diluted after being introduced via a single channel, or to be split into multiple channels without the need for individual pipetting. Flow through the multiple channels can be regulated to allow a series of sister wells or chambers to all fill prior to the fluid flowing beyond any one of the sister wells or chambers. The filling of sister wells or chambers in this manner allows all wells or chambers to undergo reactions in unison. [see McNeely, abstract]

- b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 15 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 10 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 15 obvious.

- c. The McNeely Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 15 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that McNeely does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 15 of the present application.

According to McNeely, “[t]he invention is a method of using passive stopping means in microchannels to control the flow of fluids through the microchannels The stopping means are designed to impede the flow of fluids under certain conditions thereby allowing control of the fluid. These stopping means act as passive valves because they regulate fluid flow but do not move.” [McNeely, column 5, lines 18-28] In particular, “

[a] stopping means is generated by altering the character of a microchannel in such a way as to generate a pressure barrier. A pressure barrier is made by creating an abrupt change in the capillary force a fluid experiences while flowing through a microchannel. An abrupt change in capillary force can be made by changing the diameter of the microchannel the fluid is flowing through, by changing the contact angle of the microchannel material, by changing the surface

tension of the flowing fluid, or by a combination of these methods. [McNeely, column 5, lines 50-59]

For example, “[i]n a hydrophobic material a pressure barrier can be generated by decreasing the diameter of the flow channel. This restriction (a narrowing) should be sufficient to cause fluid to flow in alternate channels having a diameter greater than the restriction means.” [McNeely, column 5, line 60-column 6, line 6] “In a hydrophilic material a pressure barrier can be generated by a channel restriction, similar to the method described for a hydrophobic material. However, in this case the fluid will not want to exit a restriction, due to the capillary forces that are holding it there.” [McNeely, column 6, lines 11-18] Alternatively, a pressure barrier can be generated in a hydrophilic material by altering the contact angle of the flow channel. [*see* McNeely, column 6, lines 21-22] Additionally, “[a] stopping means can also be generated by changing the surface tension of the fluid within the microchannel. This, also, could be realized by utilizing microfabrication techniques to deposit thin films of various salts or surfactants that are absorbed into the fluid.” [McNeely, column 6, lines 29-33] As taught by McNeely, “[i]t is advantageous to use passive fluid dynamics to control the flow of fluid in micro channels or sets of micro channels.” [McNeely, column 6, lines 38-39]

Thus, it is respectfully submitted that McNeely merely teaches the use of passive “valves” created by suitable pressure barriers to “impede the flow of fluids under certain conditions thereby allowing control of the fluid.” In particular, although these passive “valves” may regulate fluid flow, McNeely expressly teaches that the passive valves “do not move.” [*see* McNeely, column 5, lines 18-28] Rather, the passive “valves” are merely pressure barriers that impede the flow of fluid until sufficient pressure in the fluid has been reached to allow the fluid to push past the stopping means. [*see* McNeely, column 6, lines 43-46] Accordingly, it is respectfully submitted that nowhere does McNeely teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample.**

The Appellants respectfully note that the Patent Office has failed to indicate where in McNeely the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that McNeely does not address the above-identified deficiencies of Schnipelsky.

- d. Since the Combination of Schnipelsky and McNeely Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 15 Of The Present Application, The Combination Of Schnipelsky, and McNeely Does Not Render Dependent Claim 15 Obvious.

Since Schnipelsky and McNeely, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 15 of the present application, it is respectfully submitted that the combination of Schnipelsky and McNeely does not render dependent claim 15 unpatentable.

With regard to the combination of Schnipelsky and McNeely, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the second conduit of Schnipelsky et al., a valve that is responsive to hydrostatic pressure as taught by McNeely et al., in order to prevent the reagent in the second conduit from reacting with fluid in the first conduit with a valve that does not significantly affect established flow in the channel once it becomes established.” [Final Office Action, page 7, lines 5-9] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky or McNeely, or any other source, to support such an unfounded and baseless assertion.

In addition, according to M.P.E.P. § 2143.02, “[t]he prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success.” [(citations omitted)] It is respectfully noted that McNeely requires that the “passive stopping means” be used in microchannels, defined as “a channel having a diameter of from 0.1 to 1000 microns.” [McNeely, column 5, lines 18-22] The Patent Office has failed to show that the passageways taught by Schnipelsky qualify as such “microchannels” that would allow McNeely’s passive “valves” to function as intended. In addition, it respectfully noted that the external pressuring means 60 (e.g., a pressure roller) taught by Schnipelsky may need to exert a significant amount of pressure to burst seals 46 and 56 and move the fluids through the passageways of Schnipelsky’s cuvette 10. Such pressures could be too high to practically use the pressure barriers of the passive “valves” to effectively “prevent the reagent in the second conduit from reacting with fluid in the first conduit” as asserted by the Patent Office. For example, it is respectfully noted that Schnipelsky teaches the use of pinching means (e.g., pinch points P₁-P₅ illustrated in Figure 1) to prevent liquid from backwashing up to the passageway used to empty another compartment that is further downstream. [see Schnipelsky, column 11, lines 37-47] In sum, it is respectfully submitted that the Patent Office has utterly failed to show that the passive “valves” taught by McNeely would have a reasonable expectation of success in the passageways of the cuvette taught by Schnipelsky, in derogation of the Patent Office’s duties as mandated by M.P.E.P. § 2143.02.

Rather, it is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky and McNeely is a bald assertion wholly and completely without support in either Schnipelsky or McNeely. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office’s attempt to

combine Schnipelsky and McNeely for its rejection based on obviousness is clearly and unequivocally founded upon “knowledge gleaned only from applicant’s disclosure.” [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and McNeely does not render the subject matter of dependent claim 15 obvious.

Dependent claim 16 depends from claim 15, and is, therefore, patentably distinguishable over the combination of Schnipelsky and McNeely for at least those reasons stated above with regard to dependent claim 15.

For at least the foregoing reasons, it is respectfully submitted that the combination of Schnipelsky and McNeely does not render the subject matter of claims 15 and 16 unpatentable.

Hence, the subject matter of claims 15 and 16 is separately patentable for this reason.

I. Rejection Of Claim 20 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Cathey.

It is respectfully submitted that the combination of Schnipelsky and Cathey is improper. *Even if* the combination of Schnipelsky and Cathey was proper, it is respectfully submitted that Schnipelsky and Cathey, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 20 of the present application.

a. The Cathey Patent.

As understood by Appellants, Cathey is directed to a disposable diagnostic device and method of its use. According to Cathey, the device comprises a housing containing first and second flow paths orthogonal to each other. The first flow path commences at a sample addition port and continues through a transport channel that feeds sample to an incubation area by means of capillary flow. The incubation area comprises a signal producing system and is underneath an optically-clear window. The first flow path terminates in a top waste reservoir that receives sample and wash fluid. The second flow path begins on one side of the incubation area at an inlet port over a side reagent reservoir. Liquid flows along the second flow path from the side reagent reservoir across the incubation area into the side waste reservoir. The incubation area can include an agitation means for homogenous dispersion of reagent into liquid. Various reagents of a signal producing system can be contained within the device and the necessary liquids added automatically by appropriate instrumentation, so as to have the assay carried out automatically, without technician involvement, providing an accurate and sensitive determination. [see Cathey, abstract]

- b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 20 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 10 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 20 obvious.

- c. The Cathey Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 20 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Cathey does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 20 of the present application.

According to Cathey, the disposable device can include a capillary valve located adjacent to the incubation area at various positions along the first and second flow paths for enhanced control over liquid flow through the incubation area. [see Cathey, column 5, lines 36-39] “[T]he capillary valve may be positioned in the second flow path between the side reagent reservoir and the incubation area to control the flow of liquid from the side reagent reservoir into the incubation area. Further, a capillary valve may be positioned in the first flow path to control fluid flow into and/or out of the incubation area.” [Cathey, column 5, lines 39-45] Cathey teaches that the capillary valve includes a control capillary that intersects the subject flow path. The depth of the control capillary will be greater than the depth of the intersected flow path. [see

Cathey, column 5, lines 47-50] In particular, “[t]he control capillary is designed so that capillary flow in the control capillary is not impeded at the intersection with the flow path. However, capillary flow in the flow path is **impeded** at the intersection when the control capillary is **void of liquid** because of the sharp interruption in the depth of the flow path. Only when the control capillary is **full** is capillary flow in the intersected flow path **not** impeded.” [Cathey, column 5, lines 50-56]

Thus, it is respectfully submitted that Cathey teaches that the capillary valves operate in a manner that is **opposite** to the valve recited in dependent claim 20. More particularly, the capillary valve taught by Cathey impedes (“closes”) the flow of liquid when the control capillary is empty, and permits (“opens”) the flow of fluid when the control capillary is full. Accordingly, it is respectfully submitted that nowhere does Cathey teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample.**

The Appellants respectfully note that the Patent Office has failed to indicate where in Cathey the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Cathey does not address the above-identified deficiencies of Schnipelsky.

- d. Since the Combination of Schnipelsky and Cathey Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 20 Of The Present Application, The Combination Of Schnipelsky, and Cathey Does Not Render Dependent Claim 20 Obvious.

Since Schnipelsky and Cathey, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 15 of the present application, it is respectfully submitted that the combination of Schnipelsky and Cathey does not render dependent claim 20 unpatentable.

With regard to the combination of Schnipelsky and Cathey, the Patent Office asserts that one of ordinary skill in the art at the time the invention was made would have been motivated to include the dried reagent in a first conduit of Schnipelsky et al. instead of the sample compartment. One having ordinary skill would have been motivated to make such a change as mere alternative and functionally equivalent reagent distribution technique and since only the expected time at which the reagent was distributed would have been obtained. The use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on preventing inhomogeneous mixing of reagents with a sample. [Final Office Action, page 7, line 17-page 8, line 2]

It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky or Cathey, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office's stated motivation for combining Schnipelsky and Cathey is a bald assertion wholly and completely without support in either Schnipelsky or Cathey. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office's stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office's attempt to combine Schnipelsky and Cathey for its rejection based on obviousness is clearly and unequivocally founded upon "knowledge gleaned only from applicant's disclosure." [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

In addition, the Patent Office makes numerous references to “alternative and functionally equivalent reagent distribution technique[s].” [see Final Office Action, page 7, line 17-page 8, line 2] It is respectfully noted that “[i]n order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on . . . the mere fact that the components at issue are functional or mechanical equivalents.” [M.P.E.P. § 2144.06 (emphasis added)] The Patent Office’s use of equivalency is apparently based on the functional equivalence of the reagent distribution techniques. Therefore, it is respectfully submitted that the Patent Office’s determination of alleged equivalence is improper, and, therefore, traversed.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and Cathey does not render the subject matter of dependent claim 20 obvious.

Hence, the subject matter of claim 20 is separately patentable for this reason.

J. Rejection Of Claims 21-26, 28, 29, 32, And 33 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Cathey, And In Further View Of Zier And Pourahmadi.

It is respectfully submitted that the combination of Schnipelsky, Chemelli, Zier, and Pourahmadi is improper. *Even if* the combination of Schnipelsky, Chemelli, Zier, and Pourahmadi was proper, it is respectfully submitted that Schnipelsky, Chemelli, Zier, and Pourahmadi, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claims 21, 24, 25, 28, 29, and 32 of the present application.

a. The Zier Patent.

As understood by Appellants, Zier is directed to an implantable electrochemical sensor for amperometric measurements in body liquids. The sensor comprises at least one measurement electrode formed as a platinum wire, a reference electrode tubularly surrounding the measurement electrode and possibly made up of several parts and made of stainless steel containing molybdenum as an alloying component. Furthermore, a layer of an immobilized enzyme, such as glucose oxidase, is disposed on the electrodes. The sensor is intended for use for the control of blood sugar and tissue sugar in diabetics and is suitable to be employed in a portable diagnostic and/or therapeutic apparatus. [see Zier, abstract]

b. The Pourahmadi Application.

As understood by Appellants, Pourahmadi is directed to a device for separating an analyte from a fluid sample. The device comprises a cartridge having a sample port and a first flow path extending from the sample port. A microfluidic chip is positioned in the first flow path. The microfluidic chip includes an extraction chamber having an array of microstructures

for capturing the analyte from the sample as the sample flows through the extraction chamber and for subsequently releasing the captured analyte into an elution fluid as the elution fluid flows through the extraction chamber. Each of the microstructures has an aspect ratio of at least 2:1. The cartridge also includes a second flow path for eluting the captured analyte from the microfluidic chip, the second flow path diverging from the first flow path after passing through the chip. At least one flow controller directs the sample into the first flow path and the eluted analyte into the second flow path. [see Pourahmadi, abstract]

- c. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 21, 24, 25, 28, 29, and 32 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claims 21, 24, 25, 28, 29, and 32 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claims 21, 24, 25, 28, 29, and 32 obvious.

- d. The Cathey Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 21, 24, 25, 28, 29, and 32 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(I)(c) of the present Appeal Brief, it is respectfully submitted that Cathey does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in

which **the valve is closed by contact with the sample**, as recited in, for example, dependent claims 21, 24, 25, 28, 29, and 32 of the present application.

Consequently, it is respectfully submitted that Cathey does not address the above-identified deficiencies of Schnipelsky.

- e. The Zier Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 21, 24, 25, 28, 29, and 32 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Zier does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 21, 24, 25, 28, 29, and 32 of the present application.

As illustrated in Figures 1-3 of Zier, the implantable electrochemical enzyme sensors 1 comprise a thin cylindrical tube-shaped cannula 10 made of metal that contains an insulating epoxy resin filler 12, as well as one or two axially directed measurement electrodes 14, 14'. The metallic tube jacket forms at the same time the reference electrode 11' of the electrochemical sensor. [see Zier, column 6, lines 58-66] It is respectfully submitted that Zier does not teach or suggest any type of valve or other like mechanism for use in or by the sensors. Accordingly, it is respectfully submitted that nowhere does Zier teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**.

The Appellants respectfully note that the Patent Office has failed to indicate where in Zier the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Zier does not address the above-identified deficiencies of Schnipelsky and Cathey.

- f. The Pourahmadi Application Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 21, 24, 25, 28, 29, and 32 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Pourahmadi does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 21, 24, 25, 28, 29, and 32 of the present application.

According to Pourahmadi, a cartridge 101 for performing various operations on a fluid sample can include “at least one flow controller, e.g., one or more valves, flow diverters, or fluid diodes, for directing the fluid sample into the sample flow path after the sample flows through the capture component and for directing the elution fluid and eluted analyte into the elution flow path after the elution fluid flows through the capture component.” [Pourahmadi, page 2, paragraph 0016] For example, as illustrated in Figure 2, “[t]he flow controllers 41A and 41B are arranged to direct the sample into the waste chamber 139 after the sample flows through the capture component 122. The flow controllers 41A and 41B may be, e.g., valves, flow diverters, or fluid diodes.” [Pourahmadi, page 4, paragraph 0052] According to one embodiment,

[m]agnetic forces may also be used to operate small valves within the cartridge for fluid control. A small strip of magnetic material may be incorporated into the cartridge to divert the fluid flow along one particular flow path. Another possibility is to fabricate the magnetic strip in such a way that it returns to the first position when the field is removed. The strip could be fabricated in such a way as to be mechanically bistable. Application of a magnetic pulse to the strip causes a mechanical transition from the initial bistable state to the second state. In this second state, the strip diverts the fluid flow to an alternative path. An array of such valves allows complete control of the fluid motion. [Pourahmadi, page 10, paragraph 0121]

However, Pourahmadi teaches that “[a]lthough the preferred embodiment incorporates flow controllers, e.g. valves, it is possible for a continuously-flowing fluid stream to be guided, divided and diverted to various regions within the cartridge without the incorporation of valves.

In one embodiment, the fluid stream flows down a channel with relatively little flow resistance into a second region, e.g., a waste chamber.” [Pourahmadi, page 8, paragraph 0102]

Thus, *at most*, it is respectfully submitted that Pourahmadi teaches that valves can act as “flow controllers” to divert the motion of fluid in the cartridge 101. For example, the valves can be activated by magnetic forces to control the fluid motion. However, it is respectfully submitted that nowhere does Pourahmadi teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**.

The Appellants respectfully note that the Patent Office has failed to indicate where in Pourahmadi the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Pourahmadi does not address the above-identified deficiencies of Schnipelsky, Cathey, and Zier.

- g. Since the Combination of Schnipelsky, Cathey, Zier, and Pourahmadi Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 21, 24, 25, 28, 29, and 32 Of The Present Application, The Combination Of Schnipelsky, Cathey, Zier, and Pourahmadi Does Not Render Dependent Claims 21, 24, 25, 28, 29, and 32 Obvious.

Since Schnipelsky, Cathey, Zier, and Pourahmadi, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claims 21, 24, 25, 28, 29, and 32 of the present application, it is respectfully submitted that the combination of Schnipelsky, Cathey, Zier, and Pourahmadi does not render dependent claims 21, 24, 25, 28, 29, and 32 unpatentable.

With regard to the combination of Schnipelsky, Cathey, Zier, and Pourahmadi, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute for the immobilized DNA in the analyte responsive sensor of Schnipelsky et al. in view of Cathey et al., an enzyme substrate of glucose and an enzyme of

glucose oxidase in a sample as taught by Zier et al., in order to provide a compact and efficient detection of large sample volumes as taught by Pourahmadi et al.” [Final Office Action, page 8, lines 18-22] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky, Cathey, Zier, or Pourahmadi, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky, Cathey, Zier, and Pourahmadi is a bald assertion wholly and completely without support in either Schnipelsky, Cathey, Zier, or Pourahmadi. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office’s attempt to combine Schnipelsky, Cathey, Zier, and Pourahmadi for its rejection based on obviousness is clearly and unequivocally founded upon “knowledge gleaned only from applicant’s disclosure.” [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky, Cathey, Zier, and Pourahmadi does not render the subject matter of dependent claims 21, 24, 25, 28, 29, and 32 obvious.

Dependent claims 22, 23, 26, and 33 variously depend from claims 21, 25, and 32, and are, therefore, patentably distinguishable over the combination of Schnipelsky, Cathey, Zier, and Pourahmadi for at least those reasons stated above with regard to dependent claims 21, 25, and 32.

For at least the foregoing reasons, it is respectfully submitted that the combination of Schnipelsky, Cathey, Zier, and Pourahmadi does not render the subject matter of claims 21-26, 28, 29, 32, and 33 unpatentable.

Hence, the subject matter of claims 21-26, 28, 29, 32, and 33 is separately patentable for this reason.

K. Rejection Of Claim 27 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Cathey, In View Of Zier, In View Of Pourahmadi, And Further In View Of Grundig.

It is respectfully submitted that the combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig is improper. *Even if* the combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig was proper, it is respectfully submitted that Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 27 of the present application.

a. The Grundig Patent.

As understood by Appellants, Grundig is directed to an enzymatic-electrochemical affinity sensor and a one-step affinity assay for the quantitative determination of analytes in aqueous media. More specifically, the invention relates to an enzymatic-electrochemical signal amplification system for a highly sensitive indication of affinity reactions and is particularly suitable in the form of a one-step affinity sensor for *in situ* analytics. The invention is also directed to the use of phenol oxidase as a marker enzyme for the affine binding partners in an electrochemical affinity sensor or assay, and to the use of an enzyme hydrolyzing phenolic compounds as marker enzyme for the affine binding partners, in combination with a phenol oxidase as catalyst for the amplifying reaction in an electrochemical affinity assay. [see Grundig, abstract]

- b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 27 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 27 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 27 obvious.

- c. The Cathey Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 27 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(I)(c) of the present Appeal Brief, it is respectfully submitted that Cathey does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 27 of the present application.

Consequently, it is respectfully submitted that Cathey does not address the above-identified deficiencies of Schnipelsky.

- d. The Zier Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 27 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(J)(e) of the present Appeal Brief, it is respectfully submitted that Zier does not teach

or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 27 of the present application.

Consequently, it is respectfully submitted that Zier does not address the above-identified deficiencies of Schnipelsky and Cathey.

- e. The Pourahmadi Application Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 27 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(I)(c) of the present Appeal Brief, it is respectfully submitted that Pourahmadi does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 27 of the present application.

Consequently, it is respectfully submitted that Pourahmadi does not address the above-identified deficiencies of Schnipelsky, Cathey, and Zier.

- f. The Grundig Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 27 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Grundig does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 27 of the present application.

As illustrated in Figures 1 and 2 of Grundig,

[c]arbon contact paths 2, an N-methylphenazinium Reineckate-modified carbon working electrode 3, a silver/silver chloride (Ag/AgCl) reference electrode 4

surrounding the working electrode 3 in the form of a square ribbon, and an isolating layer 5 which, in addition to the surfaces of the working and reference electrodes and plug contact surfaces, covers the support, are printed consecutively on a glass fiber-epoxide resin support 1 using polymer thick-layer pastes and cured at 90° C. Directly on the measuring window surface where the working electrode 3 and the reference electrode 4 are arranged, a fixing frame 6, 7 made of plastic is clamped by appropriate shapings onto the support 1. The fixing frame includes a cylindric cavity and has regularly arranged openings 0.1 mm in diameter in its top cover 8 over a limited circular area 1.5 mm in diameter. The fixing frame is tightly packed with a sequence of different layers: Directly below the perforated circular area of the fixing frame cover 8, there is a Silopren film 9 . . . spaced apart from the cover by an annular spacer 10 . . . made of filter paper . . . The Silopren film is followed by a swellable layer 11 having a diameter of 5 mm, which consists of a filter paper coated with SANWET® IM 3900 G (Hoechst AG) and serves as sample-receiving and reservoir layer. [Grundig, column 9, lines 6-32]

It is respectfully submitted that nowhere does Grundig teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample.**

The Appellants respectfully note that the Patent Office has failed to indicate where in Grundig the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Grundig does not address the above-identified deficiencies of Schnipelsky, Cathey, Zier, and Pourahmadi.

- g. Since the Combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 27 Of The Present Application, The Combination Of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig Does Not Render Dependent Claim 27 Obvious.

Since Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to

an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 27 of the present application, it is respectfully submitted that the combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig does not render dependent claim 27 unpatentable.

With regard to the combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al. in view of Cathey et al. and further in view of Zier et al. and Pourahmadi et al., a ferrocene substrate as taught by Grundig et al., in order to modify increase the sensitivity of amperometric indication of an electrode comprising glucose oxidase.” [Final Office Action, page 9, lines 18-22] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky, Cathey, Zier, Pourahmadi, or Grundig, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig is a bald assertion wholly and completely without support in either Schnipelsky, Cathey, Zier, Pourahmadi, or Grundig. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office’s attempt to combine Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig for its rejection based on obviousness is clearly and unequivocally founded upon “knowledge gleaned only from applicant’s disclosure.”

[*see* M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky, Cathey, Zier, Pourahmadi, and Grundig does not render the subject matter of dependent claim 27 obvious.

Hence, the subject matter of claim 27 is separately patentable for this reason.

L. Rejection Of Claims 31 And 36 Under 35 U.S.C. § 103(A) As Allegedly Being Unpatentable Over Schnipelsky In View Of Pourahmadi.

It is respectfully submitted that the combination of Schnipelsky and Pourahmadi is improper. *Even if* the combination of Schnipelsky and Pourahmadi was proper, it is respectfully submitted that Schnipelsky and Pourahmadi, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claims 31 and 36 of the present application.

- a. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 31 and 36 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claims 31 and 36 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claims 31 and 36 obvious.

- b. The Pourahmadi Application Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 31 and 36 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(I)(c) of the present Appeal Brief, it is respectfully submitted that Pourahmadi does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in

which **the valve is closed by contact with the sample**, as recited in, for example, dependent claims 31 and 36 of the present application.

Consequently, it is respectfully submitted that Pourahmadi does not address the above-identified deficiencies of Schnipelsky.

- c. Since the Combination of Schnipelsky and Pourahmadi Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claims 31 and 36 Of The Present Application, The Combination Of Schnipelsky and Pourahmadi Does Not Render Dependent Claims 31 and 36 Obvious.

Since Schnipelsky and Pourahmadi, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claims 31 and 36 of the present application, it is respectfully submitted that the combination of Schnipelsky and Pourahmadi does not render dependent claims 31 and 36 unpatentable.

With regard to the combination of Schnipelsky and Pourahmadi and the rejection of dependent claim 31, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al, a surface coating that decreases non-specific binding as taught by Pourahmadi et al., in order to minimize non-specific binding and more accurately detect analyte present in the sample in low concentrations.” [Final Office Action, page 10, lines 9-12] With regard to the rejection of dependent claim 36, the Patent Office asserts that “it would have been obvious to include the filter element in the cartridge of Schnipelsky et al. between the sample holding chamber and at least one analyte sensor, and adjacent to the at least one sensor, a filter element as taught by Pourahmadi et al., in order to efficiently capture analyte. The microparticles of Pourahmadi et al. would therefore become concentrated adjacent the at least one sensor.” [Final Office Action, page 10, lines 16-20]

It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such assertions, as the Patent Office has provided no reference, citation or other actual evidence supporting such assertions and such alleged motivations to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky or Pourahmadi, or any other source, to support such unfounded and baseless assertions.

Rather, it is respectfully submitted that the Patent Office's stated motivations for combining Schnipelsky and Pourahmadi are bald assertions wholly and completely without support in either Schnipelsky and Pourahmadi. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office's stated motivations. Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manners suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office's attempt to combine Schnipelsky and Pourahmadi for its rejection based on obviousness is clearly and unequivocally founded upon "knowledge gleaned only from applicant's disclosure." [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and Pourahmadi does not render the subject matter of dependent claims 31 and 36 obvious.

Hence, the subject matter of claims 31 and 36 is separately patentable for this reason.

M. Rejection Of Claim 35 Under 35 U.S.C. § 103(a) As Allegedly Being Unpatentable Over Schnipelsky In View Of Nelson.

It is respectfully submitted that the combination of Schnipelsky and Nelson is improper. *Even if* the combination of Schnipelsky and Nelson was proper, it is respectfully submitted that Schnipelsky and Nelson, whether considered alone or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in dependent claim 35 of the present application.

a. The Nelson Patent.

As understood by Appellants, Nelson is directed to integrated microfluidic devices that comprise at least an enrichment channel and a main electrophoretic flowpath. In the integrated devices, the enrichment channel and the main electrophoretic flowpath are positioned so that waste fluid flows away from the main electrophoretic flowpath through a discharge outlet. The devices find use in a variety of electrophoretic applications, including clinical assays, high throughput screening for genomics and pharmaceutical applications, point-or-care in vitro diagnostics, molecular genetic analysis and nucleic acid diagnostics, cell separations, and bioresearch generally. [see Nelson, abstract]

b. The Schnipelsky Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 35 Of The Present Application.

Contrary to the assertions of the Patent Office, and as previously discussed at length in Section VII(C)(b) of the present Appeal Brief, it is respectfully submitted that Schnipelsky does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent

claim 35 of the present application. For at least the foregoing reasons, it is respectfully submitted that Schnipelsky does not render the subject matter of dependent claim 35 obvious.

- c. The Nelson Patent Does Not Teach Or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 35 Of The Present Application.

Contrary to the assertions of the Patent Office, it is respectfully submitted that Nelson does not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 35 of the present application.

According to Nelson, “[t]o control bulk fluid flow through the enrichment channel, e.g., to prevent waste sample from flowing into the main electrophoretic flowpath, fluid control means, e.g., valves, membranes, etc., may be associated with each of the inlets and outlets.” [Nelson, column 8, lines 52-56] In particular, as illustrated in Figure 1, “[f]or controlling fluid flow through the channel inlets and outlets, valves 8, 9 and 11 are provided.” [Nelson, column 12, lines 5-6] “Valves 8 and 9 are closed to prevent sample from flowing or ‘bleeding’ out inlet 4 or outlet 5. After the sample has flowed through channel 10, valve 11 is shut and valves 8 and 9 are opened.” [Nelson, column 12, lines 14-17] However, according to Nelson, “[t]he invention provides means for the automated electroactive control of the fluid circuitry without requiring the use of mechanical valves . . .” [Nelson, column 24, lines 14-16 (emphasis added)]

Thus, *at most*, it is respectfully submitted that Nelson teaches that the valves 8, 9, and 11 can act as “flow controllers” to control bulk fluid flow by suitably opening and closing. However, it is respectfully submitted that nowhere does Nelson teach or even suggest the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**.

The Appellants respectfully note that the Patent Office has failed to indicate where in Nelson the aforesaid claim features are taught or suggested.

Consequently, it is respectfully submitted that Nelson does not address the above-identified deficiencies of Schnipelsky.

- d. Since the Combination of Schnipelsky and Nelson Does Not Teach or Suggest At Least The Feature Of A Valve Connected To An Opening In The First Conduit, In Which The Valve Is Closed By Contact With The Sample, As Recited In Dependent Claim 35 Of The Present Application, The Combination Of Schnipelsky and Nelson Does Not Render Dependent Claim 35 Obvious.

Since Schnipelsky and Nelson, whether considered individually or in combination, do not teach or suggest at least the feature of a valve connected to an opening in the first conduit, in which **the valve is closed by contact with the sample**, as recited in, for example, dependent claim 35 of the present application, it is respectfully submitted that the combination of Schnipelsky and Nelson does not render dependent claim 35 unpatentable.

With regard to the combination of Schnipelsky and Nelson, the Patent Office asserts that “it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute for the particles in Schnipelsky et al., magnetic particles with a magnetic field as taught by Nelson et al., in order to provide a rapid and reliable method of localization of analyte.” [Final Office Action, page 11, lines 6-9] It is respectfully submitted that the Patent Office has provided absolutely no support or foundation for such an assertion, as the Patent Office has provided no reference, citation or other actual evidence supporting such an assertion and such an alleged motivation to combine these references. For example, Appellants note that the Patent Office has not even attempted to provide any citation to Schnipelsky or Nelson, or any other source, to support such an unfounded and baseless assertion.

Rather, it is respectfully submitted that the Patent Office’s stated motivation for combining Schnipelsky and Nelson is a bald assertion wholly and completely without support in either Schnipelsky or Nelson. It is respectfully submitted that the Patent Office has failed to provide support or other actual evidence, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, for the Patent Office’s stated motivation.

Rather, it is respectfully submitted that there is no teaching, suggestion or motivation, either explicitly or implicitly, to combine the references in the manner suggested by the Patent Office. Consequently, it is respectfully submitted that the Patent Office has not established a *prima facie* case of obviousness. Rather, it is respectfully submitted that the Patent Office's attempt to combine Schnipelsky and Nelson for its rejection based on obviousness is clearly and unequivocally founded upon "knowledge gleaned only from applicant's disclosure." [see M.P.E.P. § 2145] Consequently, it is respectfully submitted that the rejection entails hindsight and is, therefore, improper.

For at least the aforementioned reasons, it is respectfully submitted that the combination of Schnipelsky and Nelson does not render the subject matter of dependent claim 35 obvious.

Hence, the subject matter of claim 36 is separately patentable for this reason.

VIII. Conclusion

For the reasons presented above, the rejections of the claims are not properly founded in the statute and should be reversed.

Respectfully submitted,

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IX. APPENDIX A: Appealed Claims

1. (Canceled)

2. A cartridge for sensing at least one analyte in a sample, said cartridge comprising:

a sample holding chamber for receiving said sample and retaining said sample;

a first conduit connected to said sample holding chamber;

at least one analyte sensor,

wherein said sensor comprises an analyte-responsive surface and said surface is within said first conduit;

a second conduit for retaining a fluid,

said second conduit connected to said first conduit;

a valve connected to an opening in said first conduit,

wherein said valve is closed by contact with said sample; and

pump capable of displacing said sample from said holding chamber into said first

conduit,

said pump further capable of displacing said fluid from said second conduit into said first conduit.

3. A cartridge for sensing at least one analyte in a sample, said cartridge comprising:

a sample holding chamber for receiving said sample and retaining said sample;

a first conduit connected to said sample holding chamber;

at least one analyte sensor,

wherein said sensor comprises an analyte-responsive surface and said surface is within said first conduit;

a second conduit for retaining a fluid,

said second conduit connected to said first conduit;

a valve connected to an opening in said first conduit,

wherein said valve is closed by contact with said sample;

means for inserting at least one air segment into said first or second conduit; and

pump capable of displacing said sample from said holding chamber into said first conduit,

said pump further capable of displacing said fluid from said second conduit into said first conduit.

4. The cartridge as in claim 2 or 3 further comprising at least one sensor capable of detecting an air-liquid interface.

5. The cartridge as in claim 2 or 3 wherein said cartridge is single-use.

6. The cartridge as in claim 3 wherein said segment is a single segment or a plurality of segments.
7. The cartridge as in claim 3 wherein said segment is inserted into said first conduit.
8. The cartridge as in claim 3 wherein said segment is inserted into said second conduit.
9. The cartridge as in claim 4 wherein said at least one sensor capable of detecting an air-liquid interface is a conductimetric sensor.
10. The cartridge as in claim 2 or 3 wherein said cartridge further comprises a metering means for delivering a metered amount of said sample to said at least one analyte sensor.
11. The cartridge as in claim 10 wherein said metering means comprises a capillary stop within said first conduit.
12. The cartridge as in claim 3 wherein said means for inserting at least one air segment is selected from the group consisting of an air sac comprising a pneumatic means for

displacing air from said air sac into said second conduit, a dry chemical that produces a gas when dissolved, a plurality of electrolysis electrodes operably connected to a current source, a porous means that absorbs fluid displacing air from said porous means into said conduit, and a vent that permits an air segment to enter the fluid when said pump means moves said fluid.

13. The cartridge as in claim 2 or 3 wherein said closeable valve is selected from the group consisting of a dry sponge material coated with a fluid impermeable layer, a flap capable of blocking said valve and held open by a dry soluble compound, and a gelling polymer.

14. The cartridge as in claim 2 or 3 further comprising at least one constriction to control fluid flow within said first and second conduits.

15. The cartridge as in claim 2 or 3 wherein said second conduit further comprises a valve responsive to hydrostatic pressure.

16. The cartridge as in claim 15, wherein said valve comprises a constriction in said conduit, wherein said constriction has a fluid-contacting surface comprising a hydrophobic surface.

17. The cartridge as in claim 2 or 3 further comprising a third conduit connecting said

second conduit and an overflow chamber.

18. The cartridge as in claim 2 or 3 wherein said pump is selected from the group consisting of an air sac contacting a pneumatic means whereby pressure is applied to said air sac, a flexible diaphragm, a piston and cylinder, an electrodynamic pump, and a sonic pump.

19. The cartridge as in claim 2 or 3 in which said analyte-responsive surface comprises an antibody.

20. The cartridge as in claim 2 or 3 wherein a portion of at least one conduit further comprise at least one dry reagent capable of dissolving in said fluid or sample.

21. The cartridge as in claim 20 wherein said at least one dry reagent is an antibody-enzyme conjugate, a substrate for said antibody-enzyme conjugate, or a blocking agent.

22. The cartridge as in claim 21 wherein said at least one antibody-enzyme conjugate comprises an enzyme that is urease, glucose oxidase, peroxidase, or alkaline phosphatase.

23. The cartridge as in claim 22 wherein said substrate is urea, glucose, hydrogen peroxide, or a molecule having a phosphate or peroxide moiety.

24. The cartridge as in claim 2 or 3 wherein said at least one analyte sensor is an immunosensor.

25. The cartridge as in claim 2 or 3 wherein said fluid comprises a substrate for an antibody-enzyme conjugate.

26. The cartridge as in claim 25 wherein said substrate is cleaved to produce an electroactive product.

27. The cartridge as in claim 26 wherein said substrate is a ferrocene or p-aminophenol phosphate.

28. The cartridge as in claim 2 or 3 wherein said at least one analyte sensor is an amperometric sensor, a potentiometric sensor, or a reference sensor.

29. The cartridge as in claim 2 or 3 further comprising one or more mechanical and electrical connections for insertion of said cartridge into a reading apparatus.

30. The cartridge as in claim 2 or 3 wherein said at least one analyte sensor is formed

on a substantially planar surface.

31. The cartridge as in claim 2 or 3 further comprising a surface coating that decreases non-specific binding of a substance therein.

32. The cartridge as in claim 2 or 3 further comprising an enzyme and a substrate capable of regenerating a product consumed by contact with said at least one analyte sensor, whereby a signal from said sensor is increased.

33. The cartridge as in claim 32 wherein said enzyme is glucose oxidase and said substrate is D-glucose.

34. The cartridge as in claim 2 or 3 further comprising mobile microparticles capable interacting with said analyte and further comprising means for localizing said microparticles to said at least one sensor.

35. The cartridge as in claim 34, wherein said microparticles are magnetic, and said means for localizing said microparticles is a magnet field.

36. The cartridge as in claim 34, further comprising a filter element interposed

between said sample holding chamber and said at least one analyte sensor, and adjacent said at least one sensor,

whereby said microparticles are concentrated adjacent said at least one sensor.

37. - 55. (Canceled)

56. The cartridge as in claim 2 or 3 wherein said sample holding chamber further comprises a closure means.

57. - 62. (Canceled)

Application No. 10/087,730
Attorney Docket No. 215105.00800

X. APPENDIX B: Evidence

Annotated copy of the Final Office Action.



UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,730	03/05/2002	Graham Davis	215105.00800	8527
27160	7590	03/23/2006	EXAMINER	
KATTEN MUCHIN ROSENMAN LLP			YU, MELANIE J	
525 WEST MONROE STREET			ART UNIT	PAPER NUMBER
CHICAGO, IL 60661-3693			1641	

DATE MAILED: 03/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/087,730	DAVIS ET AL.
	Examiner Melanie Yu	Art Unit 1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 17 January 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 2-36, 46, 47 and 56 is/are pending in the application.
- 4a) Of the above claim(s) 46 and 47 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 2-36 and 56 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 22 April 2002 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

1. Applicant's amendment filed 17 January 2006 has been entered. Claims 2-36 and 46-56 are currently pending in this application. Claims 46-56 have been withdrawn from consideration as drawn to a non-elected invention.

5 Claim Objections

1. Claims 46 and 47 objected to because of the following informalities: the status identifiers for claims 46 and 47 are unclear. The application identifies claims 37-55 as being canceled, but then recites a second request for rejoinder for claims 46-47. It is unclear whether claims 46-47 are pending and withdrawn or whether claims 46-47 have been canceled. Appropriate correction

10 is required.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 2, 5, 14, 17, 18, 19, 30, 34 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Schnipelsky et al. (US 5,229,297).

15 Schnipelsky et al. teach a cartridge (10, Fig. 1) comprising: a sample holding chamber for receiving a sample and retaining the sample (26, Fig. 2; col. 13, lines 30-40); a first conduit connected to the sample holding chamber (channels 44, 54 and 40 comprise a first conduit, Fig. 1; col. 10, lines 47-61); at least one analyte sensor, wherein the sensor comprises an analyte responsive surface and the surface is within the first conduit (detection site, 40, Fig. 1 is within first conduit; col. 7, lines 38-43; col. 12, lines 36-48); a second conduit, which is connected to the first conduit (48, second conduit, connected to first conduit, 44, 54 and 40, Fig. 1; col. 10,

1 lines 47-61); a valve connected to an opening in the first conduit, wherein the valve is closed by contact with the sample (check valve present in first conduit, col. 10, lines 43-46; check valve closes upon contact with sample moving back through the conduit, col. 14, lines 42-49); and a pump capable of displacing the sample from the holding chamber into the first conduit, the pump

5 further capable of displacing the fluid from the second conduit into the first conduit (cuvette is flexible and pumps fluid into channels when depressed, col. 10, line 62-col. 11, line 10).

Although Schnipelsky et al. do not specifically teach a second conduit capable of fluid retention, the conduit does not appear to require any further properties to retain fluid, and therefore the conduit of Schnipelsky et al. would be capable of retaining fluid.

10 Claim 5 fails to recite any structural limitations required in order for the cartridge to be single use. Therefore, since the cartridge of Schnipelsky et al. teaches the structural limitations recited in claim 2, the cartridge is capable of being used only once prior to disposal.

Regarding claim 14, Schnipelsky et al. teach at least one constriction to control fluid flow within the first and second conduits (pinch point, col. 12, 19-35).

15 With respect to claim 17, Schnipelsky et al. teach a third conduit connecting the second conduit to an overflow chamber (third conduit 42, connects both first and second conduit to an overflow chamber 43, Fig. 2; col. 10, lines 39-45), but does not exclude connection of the second conduit to the third conduit.

Regarding claim 18, Schnipelsky et al. teach a pump being a flexible diaphragm (26, 30, 20 Fig. 1; flexible compartments, col. 9, line 63-col. 10, line 12).

With respect to claim 19, Schnipelsky et al. teach the analyte-responsive surface comprising an antibody (biotin, col. 6, lines 45-49; col. 7, lines 39-43).

Regarding claims 30 and 34, Schnipelsky et al. teach at least one analyte sensor formed on a substantially planar surface (40, Fig. 2) and mobile microparticles capable of interacting with the analyte and further comprising means for localizing the particles to the at least one sensor (col. 6, lines 49-60).

5 Regarding claim 56, Schnipelsky et al. teach the sample holding chamber further comprising a closure means (temporary seal, 46, Fig. 1; col. 10, lines 50-52).

Claim Rejections - 35 USC § 103

2. Claims 3, 6-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297), as applied to claim 2, in view of Chemelli (US 5,254,479).

10 Schnipelsky et al., as applied to claim 2, teach a cartridge comprising: a sample holding chamber, a first conduit, at least one analyte sensor, a second conduit, a valve and a pump. However, Schnipelsky et al. fail to teach means for inserting at least one air segment into the first or second conduit.

Chemelli teaches a means for inserting at least one air segment into a first or second 15 conduit (col. 4, lines 39-44; col. 5, lines 11-23, can be first or second conduit because roller continues to next location which contains an air pocket, the air pockets of each location are released, and therefore air pockets are inserted into both the first and second conduits (col. 5, lines 11-23), in order to control incubation time.

Therefore it would have been obvious to one having ordinary skill in the art at the time 20 the invention was made to include in the cartridge of Schnipelsky et al., means for inserting at least one air segment into the first or second conduit as taught by Chemelli, in order to prevent interference of air pockets or bubbles with the detection chamber.

With respect to claim 12, Chemelli teaches a pneumatic means for displacing air from the air sac into the second conduit (col. 5, lines 11-23).

3. Claims 4 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297) in view of Chemelli (US 5,254,479), as applied to claim 3, and further in view of Zelin (US 5,821,399).

Schnipelsky et al. in view of Chemelli, as applied to claim 2, teach a cartridge for sensing at least one analyte with a means for inserting at least one air segment into the first or second conduit, but fail to teach at least one sensor capable of detecting an air-liquid interface.

Zelin teaches a cartridge comprising air segments inserted into conduits (col. 3, lines 34-42) and a conductivity sensor capable of detecting an air-liquid interface (col. 4, lines 40-67), in order to displace calibrating fluid and separate calibrating fluid from a blood test sample.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al. in view of Chemelli, a conductivity sensor as taught by Zelin, in order to increase the consistency and reliability of the output measurements by ensuring that all air is out of the detection chamber while liquid reactions are taking place.

4. Claims 10 and 11 rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297), as applied to claim 2, in view of Opalsky et al. (US 6,438,498).

20 Schnipelsky et al., as applied to claim 2, teach a cartridge for sensing at least one analyte, but fail to teach a means for metering.

| Opalsky et al. teach a means for metering involving a capillary stop in a first conduit in
order to adequately fill a sensor channel (col. 10, lines 38-col. 11, line 10).

Therefore it would have been obvious to one having ordinary skill in the art at the time
the invention was made to include in the cartridge of Schnipelsky et al., a means for metering as
5 taught by Opalsky et al., in order to regulate the amount of volume entering the detection
chamber.

5. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al.
(US 5,229,297) in view of Wozniak et al. (US 4,781,683).

Schnipelsky et al. teach a cartridge comprising a valve connected to an opening in the
10 first conduit wherein the valve is closed by contact with the sample, but fail to teach the valve
being a gelling polymer.

Wozniak et al. teach a closable valve of a gelling polymer closed by contact with the
fluid sample (col. 2, lines 52-68), in order to prevent reuse of a syringe.

Therefore it would have been obvious to one having ordinary skill in the art at the time
15 the invention was made to substitute for the one-way check valve of Schnipelsky et al., a gelling
polymer closed by contact with the fluid sample as taught by Wozniak et al., in order to provide
a low cost one-way valve that does not require mechanical components.

6. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over
Schnipelsky et al. (US 5,229,297), as applied to claim 2, in view of McNeely et al. (US
20 6,296,020).

Schnipelsky et al. teach a cartridge comprising a second conduit, but fail to teach a valve
in the second conduit.

| McNeely et al. teach a valve in a second conduit that is responsive to hydrostatic pressure, wherein the valve is a constriction having a fluid-contacting surface comprising a hydrophobic surface (col. 4, lines 14-20), in order to move fluid through a circuit in a specific manner (col. 1, lines 49-52).

5 Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the second conduit of Schnipelsky et al., a valve that is responsive to hydrostatic pressure as taught by McNeely et al., in order to prevent the reagent in the second conduit from reacting with fluid in the first conduit with a valve that does not significantly affect established flow in the channel once it becomes established.

10 7. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297), as applied to claim 2, in view of Cathey et al. (US 5,503,985).

Schnipelsky et al., as applied to claim 2, teach a compartment comprising dried reagents capable of dissolving in the sample (col. 10, lines 13-16), but fail to teach a portion of at least one conduit comprising at least one dry reagent.

15 Cathey et al. teach a device with compartment (incubation area) comprising a dried reagent, wherein the dried reagent may instead be in a channel (col. 7, lines 12-19), in order to.

Therefore one of ordinary skill in the art at the time the invention was made would have been motivated to include the dried reagent in a first conduit of Schnipelsky et al. instead of the sample compartment. One having ordinary skill would have been motivated to make such a

20 change as mere alternative and functionally equivalent reagent distribution technique and since only the expected time at which the reagent was distributed would have been obtained. The use

of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on preventing inhomogeneous mixing of reagents with a sample.

8. Claims 21-26, 28, 29, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297) in view of Cathey et al. (US 5,503,985), as applied to claim 20, and further in view of Zier et al. (US 4,919,141) and Pourahmadi et al. (US 2002/0055167).

Schnipelsky et al. in view of Cathey et al., as applied to claim 20, teach a cartridge comprising an analyte responsive surface and a conduit comprising at least one dry reagent, but fail to teach the surface comprising an antibody-enzyme conjugate.

10 Zier et al. teach an antibody enzyme conjugate wherein an enzyme is glucose oxidase (col. 3, lines 35-44) and a substrate of D-glucose (col. 7, line 63-col. 8, line 5), in order to detect diabetes. However, Zier et al. fail to teach motivation to use a D-glucose substrate and glucose oxidase enzyme in the cartridge of Schnipelsky et al.

Pourahmadi et al. teach that cartridges used for DNA detection can also be used for protein capture and detection in a sample (par. 43 and 46), wherein a dry reagent is either one for DNA purification or an antibody-enzyme conjugate (par. 87), in order to provide efficient detection of large sample volumes.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute for the immobilized DNA in the analyte responsive sensor of Schnipelsky et al. in view of Cathey et al., an enzyme substrate of glucose and an enzyme of glucose oxidase in a sample as taught by Zier et al., in order to provide a compact and efficient detection of large sample volumes as taught by Pourahmadi et al.

| Regarding claims 25, 26, 28 and 29, Zier et al. teach the blood fluid comprising a substrate for an antibody-enzyme conjugate (col. 6, lines 4-8) wherein the substrate is cleaved to produce an electroactive product (col. 7, line 63-col. 8, line 13). Zier et al. also teach the analyte sensor being an amperometric sensor (col. 4, lines 54-62), with a plurality of mechanical and electrical connections (col. 7, lines 45-62).

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Regarding claim 32, Zier et al. teach an enzyme and a substrate capable of regenerating a product consumed by contact with the at least one analyte sensor, whereby a signal from the sensor is increased (col. 7, line 63-col. 8, line 13).

9. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297) in view of Cathey et al. (US 5,503,985) and further in view of Zier et al. (US 4,919,141) and Pourahmadi et al. (US 2002/0055167), as applied to claim 26, and further in view of Grundig et al. (US 6,221,238).

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Schnipelsky et al. in view of Cathey et al. and further in view of Zier et al. and Pourahmadi et al., as applied to claim 26, teach a cartridge wherein a substrate is cleaved to produce an electroactive product, but fail to teach a substrate of ferrocene.

Grundig et al. teach a ferrocene substrate in order to provide a redox-active label of an antigen (col. 1, lines 58-62).

20

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the cartridge of Schnipelsky et al. in view of Cathey et al. and further in view of Zier et al. and Pourahmadi et al., a ferrocene substrate as taught by Grundig et al., in order to modify increase the sensitivity of amperometric indication of an electrode comprising glucose oxidase.

1 10. Claims 31 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297), as applied to claim 2, in view of Pourahmadi et al. (US 2002/0055167).

Schnipelsky et al., as applied to claim 2, teach a cartridge, but fail to teach a surface coating that decreases non-specific binding.

5 Pourahmadi et al. teach a cartridge comprising a surface coating that decreases non-specific binding of a substance (par. 101), in order to prevent adhesion of nucleic acids to a cartridge surface.

Therefore it would have been obvious to one having ordinary skill in the art at the time 10 the invention was made to include in the cartridge of Schnipelsky et al., a surface coating that decreases non-specific binding as taught by Pourahmadi et al., in order to minimize non-specific binding and more accurately detect analyte present in the sample in low concentrations.

With respect to claim 36, Pourahmadi et al. teach a filter element interposed between the sample holding chamber and the at least one analyte sensor (par. 51) in order to capture desired 15 analyte.

Therefore, it would have been obvious to include the filter element in the cartridge of Schnipelsky et al. between the sample holding chamber and at least one analyte sensor, and adjacent to the at least one sensor, a filter element as taught by Pourahmadi et al., in order to efficiently capture analyte. The microparticles of Pourahmadi et al. would therefore become 20 concentrated adjacent the at least one sensor.

11. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schnipelsky et al. (US 5,229,297), as applied to claim 34, in view of Nelson et al. (US 6,074,827).

| Schnipelsky et al., as applied to claim 34, teach a cartridge comprising a microparticle to
localize a DNA strand to the sensor (col. 6, lines 29-43), but fail to teach magnetic microparticles
and a magnetic field for localizing the microparticles to the sensor.

5 Nelson et al. teach a magnetic microparticle and a magnetic field for localizing a
microparticle (col. 6, lines 30-45), in order to retain analyte in an enrichment channel.

Therefore it would have been obvious to one having ordinary skill in the art at the time
the invention was made to substitute for the particles in Schnipelsky et al., magnetic particles
with a magnetic field as taught by Nelson et al., in order to provide a rapid and reliable method
of localization of analyte.

| 10 *Response to Arguments*

12. Applicant's arguments filed 17 January 2006 have been fully considered but they are not
persuasive. Applicant argues that the one-way check valve of Schnipelsky is not "closed" within
the meaning of the claimed invention because the check valve permits downstream flow, while
restricting upstream flow. It is noted that the feature upon which applicant relies, applicants'
15 closable valve, once closed by contact with the sample, is sealed, are not recited in the rejected
claim(s). Although the claims are interpreted in light of the specification, limitations from the
specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26
USPQ2d 1057 (Fed. Cir. 1993). The check valve of Schnipelsky reads on the instant claims
because the check valve is closed by contact with the sample in an upstream manner. The instant
20 claims do not specifically require a valve closed by the sample that prevents both upstream and
downstream flow.

1 13. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

5 14. In response to applicant's argument that Schnipelsky and Wozniak is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if 10 not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the references of Wozniak and Schnipelsky both teach techniques that prevent fluid from flowing in a certain direction in a fluidic device. Different international and domestic classifications and fields of 15 search of two inventions do not sufficiently demonstrate nonanalogous art.

15 15. In response to applicant's argument that there is no motivation to combine the references of Schnipelsky and Wozniak because the valve of Wozniak needs to permit at least a downstream flow while preventing an upstream backwash in order to be substituted for the one way check valve of Schnipelsky, the examiner recognizes that obviousness can only be 20 established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.

| See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347,
21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the valve of Wozniak is capable of permitting
downstream flow until all fluid has flowed downstream and then prevents any fluid from moving
upstream or downstream. The cartridge of Schnipelsky requires that fluid pass through the
5 conduit, but not flow upstream through the conduit, since Schnipelsky does not require a second
fluid to be passed through the conduit, the valve of Wozniak would be capable of performing this
function. Applicant asks "why one of ordinary skill would ignore the teachings of the primary
reference, which calls for a one-way check valve, and use anything other than a one-way valve?"
In response to applicant's question, one of ordinary skill would be motivated to use the valve of
10 Wozniak to stop fluid from flowing upstream through the conduit instead of the one-way check
valve of Schnipelsky, because a gelling polymer is both less complicated in structure, easier to
produce and lower cost than a one-way check valve. Therefore it would have been obvious to
one having ordinary skill in the art to use a gelling polymer instead of a one-way check valve to
prevent fluid that has flowed downstream through a conduit from moving back upstream.

15

Conclusion

No claims are allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time
policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE
20 MONTHS from the mailing date of this action. In the event a first reply is filed within TWO
MONTHS of the mailing date of this final action and the advisory action is not mailed until after
the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

| will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the

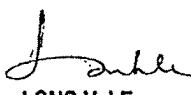
| D organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

15 system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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XI. APPENDIX C: Related Proceedings

None.